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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 C.F.R. §1.53(b)(2)

Atty. Docket: SCHROTZ-KING1

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TITLE OF THE INVENTION (280 characters max)

SURFACE-LOCATED *CAMPYLOBACTER JEJUNI* POLYPEPTIDES

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ENCLOSED APPLICATION PARTS (check all that apply)

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Respectfully submitted,

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Surfac -located *Campylobact r jejuni* polypeptides

Field of the invention

The present invention relates to cell-surface-located polypeptides of Campylobacter jejuni and to fragments and variants thereof. Furthermore, the invention relates to polynucleotides encoding the polypeptides of the invention, and to vectors and recombinant viruses or recombinant cells expressing these. The invention also relates to use of the polypeptides and of antibodies directed against these in passive and active immunisation/vaccination and in diagnostic methods. Use of the polypeptides of the invention in methods for the identification of compounds with anti-Campylobacter jejuni activity is also described.

Background of the invention

Occurrence of Campylobacter infections

Campylobacter, a Gram–negative microaerophilic bacterium, was first identified as a human pathogen in 1973. It has since become the most common bacterial cause of diarrhoeal illness in the developed world, causing more disease than the more traditionally recognised food-borne pathogens, Shigella species (spp). and Salmonella spp. combined. Of the different disease-causing Campylobacter strains, C. jejuni is the most important, being responsible for 99% of cases of campylobacteriosis. At a global level, surveillance has indicated a steady rise in the number of reported cases of campylobacteriosis since this organism was first recognised as a pathogen. Indeed, the World Health Organisation now recognises bacteria causing campylobacteriosis to be the most important agents of enteritis in the world. International public health officials estimate that C. jejuni alone causes 400 to 500 million cases of diarrhoea world-wide each year, and it is the number one food-borne pathogen in the U.S. Recent data for the year 2000 illustrate the significance of Campylobacter with respect to other more publicised causes of food borne illness. Campylobacter accounts for more cases, hospitalisations and deaths than Salmonella or E. coli-mediated food-borne illnesses. Amongst the data set, Campylobacter accounts for greater than 55% of cases and 33% of hospitalisations.

Symptoms of Campylobacter infections

Diarrhoea is the most consistent and prominent manifestation of campylobacteriosis. It is often bloody. Typical symptoms of C. jejuni infection also include fever, nausea,

vomiting, abdominal pain, headache, and muscle pain. A majority of cases are mild and do not require hospitalisation and may be self-limited. However, C. jejuni infection can be severe and life-threatening. Death is more common when other diseases (e.g. cancer, liver disease, and immunodeficiency-related diseases) are present. Children under the age of five and young adults aged 15-29 are the age groups most frequently affected. The incubation period (the time between exposure on onset of the first symptom) is typically two to five days, but onset may occur in as few as 2 days or as long as 10 days after ingestion. The illness usually lasts no more than one week; however, severe cases may persist for up to three weeks (CDC Guidelines for confirmation of food-borne disease outbreaks. MMWR, 1996; 45:59).

Long-term consequences of Campylobacter

Campylobacter infection can sometimes have long-term consequences. Some patients may develop a disease, called Guillain-Barré syndrome, that affects the nerves of the body following campylobacteriosis. Although rare, it is the most common cause of acute generalised paralysis in the Western world. It begins several weeks after the diarrhoeal illness in a small minority of Campylobacter patients. It occurs when a person's immune system generates antibodies against components of Campylobacter and these antibodies attack components of the body's nerve cells because they are chemically similar to bacterial components.[1] Guillain-Barré syndrome begins in the feet and spreads up the body. Prickling sensations give way to weakness that may lead to paralysis. It lasts for weeks to months and often requires intensive care. Full recovery is common, however patients may be left with severe neurological damage. Approximately 15% of Guillain-Barré patients remain bedridden or wheelchair-bound after one year. It is estimated that approximately one in every 1000 (0.1%) reported campylobacteriosis cases leads to Guillain-Barré syndrome. As many as 40% of Guillain-Barré syndrome cases in the UK occur following campylobacteriosis.[2]

Miller Fisher Syndrome is another, related neurological syndrome that can follow campylobacteriosis and is also caused by immunologic mimicry.[1] In Miller Fisher syndrome, the nerves of the head are affected more than the nerves of the body.

Another chronic condition that may be associated with Campylobacter infection is an arthritis called Reiter's syndrome. This is a reactive arthritis that most commonly affects large weight-bearing joints such as the knees and the lower back.

It is a complication that is strongly associated with a particular genetic make-up; persons who have the human lymphocyte antigen B27 (HLA-B27) are most susceptible.

In addition, Campylobacter may also cause appendicitis or infect the abdominal cavity (peritonitis), the heart (carditis), the central nervous system (meningitis), the gallbladder (cholecystitis) the urinary tract, and the blood stream.

References:

1. Ang CW et al. (2001) Infect Immun.69(4):2462-2469.
2. Rees et al. (1995) N Engl J Med 333:1374-1379.

Treatment of campylobacteriosis

Patients with campylobacteriosis should drink plenty of fluids as long as the diarrhoea lasts in order to maintain hydration. Antidiarrhoeal medications such as loperamide may allay some symptoms. Campylobacter is usually a self-limited illness, but when it is identified, specific treatment with antibiotics is indicated, as treatment may shorten the course of the illness. In more severe cases of gastroenteritis, antibiotics are usually begun before culture results are known. Macrolide antibiotics (erythromycin, clarithromycin, or azithromycin) are the most effective agents for C. jejuni. Fluoroquinolone antibiotics (ciprofloxacin, levofloxacin, gatifloxacin, or moxifloxacin) can also be used.

However, resistance of Campylobacter to antimicrobial agents has been reported in many countries and is on the rise (Pedungton and Kaneene (2003) J. Vet. Med. Sci. 65(2):161-170). Quinolone-resistance is on the rise in Europe, Asia and the US. The increase of resistance is at least partially related to the use of antibiotics in poultry feed (Smith et al. (1999) N Engl J Med 340:1525-1532.

Novel strategies for the treatment, prevention and diagnosis of Campylobacter

Because of the increase in incidence and the widespread occurrence of resistance, there is a considerable need for the development of new effective products for the treatment and prevention of Campylobacter infections. On one hand, due to the occurrence of resistance, there is a need for novel anti-Campylobacter compounds. On the other hand, observational and experimental studies have provided evidence of acquired immunity developing in humans, lending support to the concept of vaccine development, in particular for risk groups (Scott and Tribble (2000) In: Campylobacter, 2nd ed. Ed. by. Nachamkin and Blaser, American Society for Mi-

crobiology, pp. 303-319). In addition, there is a need for novel rapid and reliable methods for diagnosis of Campylobacter infections.

These objectives can be accomplished through the identification and use of suitable Campylobacter jejuni polypeptides that can function as targets, i.e. targets for the immune system and/or for antibodies, targets for cytotoxic inhibitors, or targets for indicator moieties in diagnosis.

Summary of the invention

The present application relates to surface-located polypeptides of Campylobacter jejuni. In the context of this application, a 'surface-located' polypeptide is defined as a polypeptide which is at least partially (i.e. part of the polypeptide chain and/or part of the population of polypeptide molecules) localised outside the outer membrane of a Campylobacter jejuni cell. Thus, a surface-located polypeptide is a polypeptide which is fully or partially exposed to the space outside the outer-membrane. Surface-located polypeptides furthermore include all polypeptides or polypeptide fragments that can be identified in fractions obtained by low-pH surface-protein extraction as described herein.

Surface-located polypeptides are attractive targets for antibacterial therapy and/or diagnosis of bacterial infection, since the exposure of such polypeptides to the extracellular space means that compounds that interact with these polypeptides (e.g. compounds used to prevent, treat or diagnose bacterial infections) often do not need to enter or pass the outer membrane to be effective.

The determination of cell-surface localisation of a Campylobacter jejuni polypeptide can at present only be done experimentally and not by bioinformatics, as no common sorting signals or motifs are known for this localisation. It is possible to predict with some degree of certainty whether or not polypeptides enter the periplasm, but no general motif has been identified for surface-localisation of polypeptides, and therefore it is not possible to predict from the sequence alone whether any given periplasmic (or non-periplasmic) polypeptide will be transported to the surface. The number of confirmed surface polypeptides is relatively low in Campylobacter jejuni and includes mostly flagella structural proteins and a small number of non-flagella related surface proteins, such as PEB1-4.

The inventors have identified 51 different polypeptides in cell-surface fractions of Campylobacter jejuni. The method that was employed identifies polypeptides that are expressed at a relatively high level. The combination of being surface-

exposed and being present in relatively high amounts makes these polypeptide highly suitable as targets for antibodies and thus for use in passive or active immunisation/vaccination. Fifteen of the 51 surface-located polypeptides that were identified (SEQ ID NO:37-51) have previously been described amongst more than 36,000 other loci as hits in homology searches using essential genes from other bacteria, see WO 02/077183. While WO 02/077183 is mostly directed towards inhibition of gene expression using antisense constructs, WO 02/077183 also describes the possibility of generating antibodies specific for any of the more than 36,000 polypeptides and the possibility of generating an immune response using any of the more than 36,000 polypeptides. However, WO 02/077183 does not describe an identification of the subcellular localisation of the identified polypeptides nor a determination of their expression levels. Thus, since most of the more than 36,000 polypeptides will not be surface-exposed and/or not expressed at sufficient levels, the large majority of the polypeptides identified in WO 02/077183 will not be suitable for generating a protective immune response in a host organism, because antibodies directed against them will not bind to an intact bacterial cell and/or because too few binding sites will be present per cell. Thus, the teaching of WO 02/077183 does not enable the skilled person to identify the minority of polypeptides amongst the more 36,000 that can be used to generate a protective immune response.

The combination of being surface-exposed and being present in relatively high amounts also makes the 51 polypeptides identified by the inventors highly suitable as targets for diagnosis of campylobacteriosis, allowing detection of intact cells with high sensitivity. In addition, the surface-localisation of the 51 polypeptides makes them suitable as targets for inhibitors. Such inhibitors may be bactericidal or bacteristatic or prevent interaction of Campylobacter jejuni with the host organism (virulence).

Definitions

- Vaccine - is used to indicate a composition capable of inducing a protective immune response against a microorganism in a human being or animal.
- Protective immune response – is used to indicate an immune response (humoral/antibody and/or cellular) inducing memory in an organism, resulting in the infectious agent, herein Campylobacter jejuni, being met by a secondary rather than a primary response, thus reducing its impact on the host organism.

- Polypeptide – unless specified otherwise, the term 'polypeptide' when used herein can also refer to a variant or fragment of a polypeptide. Preferred polypeptides are antigenic polypeptides.
- Fragment – is used to indicate a non-full length part of a polypeptide. Thus, a fragment is itself also a polypeptide.
- Variant – a 'variant' of a given reference polypeptide refers to a polypeptide that displays a certain degree of sequence identity to said reference polypeptide but is not identical to said reference polypeptide.
- Antigen / antigenic / antigenicity / immunogen / immunogenic / immunogenicity – all refer to the capability of inducing an immune response.
- Immunogenic carrier – refers to a compound which directly or indirectly assists or strengthens an immune response.
- Expression vector - refers to a, preferably recombinant, plasmid or phage or virus to be used in production of a polypeptide from a polynucleotide sequence. An expression vector comprises an expression construct, comprising an assembly of (1) a genetic element or elements having a regulatory role in gene expression, for example, promoters or enhancers, (2) a structural or coding sequence which is transcribed into mRNA and translated into protein, and which is operably linked to the elements of (1); and (3) appropriate transcription initiation and termination sequences.
- Binding partner - of a polypeptide refers to a molecule that can bind to said polypeptide. Such binding can be indirect, through another molecule, but is preferably direct. A binding partner can be any type of molecule, such as e.g. small hydrophobic molecules or e.g. a cellular or extracellular macromolecule, such as a protein, a carbohydrate or a nucleic acid. Preferred types of binding partners include antibodies, ligands or inhibitors.
- Plurality - the term 'plurality' indicates more than one, preferably more than 10.
- Indicator moiety - the term 'indicator moiety' covers a molecule or a complex of molecules that is capable of specifically binding a given polypeptide and/or cell, and is capable of generating a detectable signal. Preferably, the indicator moiety is an antibody or includes an antibody molecule. Thus, a preferred indicator moiety is an antibody coupled to or in complex with a detectable substance.
- Host-derived molecule or host molecule - refers to a molecule which is normally found in a host organism that can be infected with *C. jejuni*. A host-derived molecule is preferably a host polypeptide, preferably a human polypeptide.

- Antibody - the term 'antibodies' when used herein is intended to cover antibodies as well as functional equivalents thereof. Thus, this includes polyclonal antibodies, monoclonal antibodies (mAbs), humanised, human or chimeric antibodies, single-chain antibodies, and also binding fragments of antibodies, such as Fab fragments, $F(ab')_2$ fragments, fragments produced by a Fab expression library, anti-idiotypic antibodies, hybrids comprising antibody fragments, and epitope-binding fragments of any of the these. The term also includes multivalent, multispecific, such as bispecific antibodies and mixtures of monoclonal antibodies.
- Dissociation constant, Kd, is a measure to describe the strength of binding (or affinity or avidity) between macromolecules, for example an antibody and its antigen. The smaller Kd the stronger binding.
- Isolated - used in connection with polypeptides and polynucleotides disclosed herein 'isolated' refers to these having been identified and separated and/or recovered from a component of their natural, typically cellular, environment. Contaminant components of the natural environment are materials that would typically interfere with diagnostic or therapeutic uses for the polypeptide, and may include enzymes, hormones, and other proteinaceous or non-proteinaceous solutes. Polypeptides and polynucleotides of the invention are preferably isolated; and vaccines and other compositions of the invention preferably comprise isolated polypeptides and/or isolated polynucleotides.

Detailed description

Figures

Figure 1 and 2 show Western blot analyses using purified recombinant protein and dilutions of serum samples of immunised animals.

Vaccines and methods of vaccination of the invention

The goal of vaccination or active immunisation is to provide protective immunity by inducing a memory response to an infectious microorganism using an antigenic or immunogenic composition. Thus, a vaccine is a composition capable of inducing a protective immune response against a microorganism in a human being or animal. Such an immune response can be a cellular response and/or a humoral response, e.g. a specific T cell response or an antibody response.

In a first main aspect, the present invention relates to a (recombinant) vaccine comprising a pharmaceutically-acceptable carrier and any one or more of the following:

- a polypeptide comprising a sequence having at least 95% sequence identity to any of the sequences selected from the group of surface-located Campylobacter jejuni polypeptides of SEQ ID NO:1-51, such as any of the sequences of SEQ ID NO:1-36 or any of the sequences of SEQ ID NO:37-51; or comprising an antigenic fragment of any of said sequences,
- a polynucleotide comprising a sequence encoding said polypeptide,
- an expression vector comprising a sequence encoding said polypeptide, or
- a recombinant virus or recombinant cell comprising said polynucleotide or said expression vector.

In other words, the phrase:
'a polypeptide comprising a sequence having at least 95% sequence identity to any of the sequences selected from the group of surface-located Campylobacter jejuni polypeptides of SEQ ID NO:1-51, such as any of the sequences of SEQ ID NO:1-36 or any of the sequences of SEQ ID NO:37-51'
is directed to:
'a polypeptide comprising any of the sequences selected from the group of surface-located Campylobacter jejuni polypeptides of SEQ ID NO:1-51, such as any of the sequences of SEQ ID NO:1-36 or any of the sequences of SEQ ID NO:37-51 or a polypeptide comprising a variant of any of said sequences, wherein the variant has at least 95% sequence identity to said sequence.'

The vaccine may only comprise one polypeptide selected from the group of SEQ ID NO:1-51 or a fragment or variant thereof. However, in other embodiments, the vaccine comprises more than one polypeptide of the group of SEQ ID NO:1-51 and/or more than one fragment of a polypeptide selected from the group of SEQ ID NO:1-51. Thus, the vaccine according to the invention may comprise more than one, such as 2, for example 3, such as 4, for example 5, such as 6, for example 7, such as 8, for example 9, such as 10, such as a number of polypeptides and/or fragments in the range of from 5 to 10, or more than 10, such as for example in the range of from

10 to 20, different polypeptides selected from the group of SEQ ID NO:1-51 or fragments thereof.

Similarly, the vaccine may only comprise one polynucleotide, one expression vector or one recombinant virus or recombinant cell of the invention. However, in other embodiments, the vaccine comprises more than one polynucleotide, one expression vector or one recombinant virus or recombinant cell of the invention. Thus, the vaccine according to the invention may comprise more than one, such as 2, for example 3, such as 4, for example 5, such as 6, for example 7, such as 8, for example 9, such as 10, or more than 10, such as for example in the range of from 10 to 20, different polynucleotides, expression vectors or recombinant viruses or recombinant cells of the invention as described herein.

Furthermore, in some embodiments, a recombinant cell of the invention may express more than one polypeptide of the group of SEQ ID NO:1-51 and/or more than one fragment of a polypeptide selected from the group of SEQ ID NO:1-51. Thus, the vaccine according to the invention may comprise a recombinant cell comprising more than one, such as 2, for example 3, such as 4, for example 5, such as 6, for example 7, such as 8, for example 9, such as 10, such as a number of polypeptides and/or fragments in the range of from 5 to 10, or more than 10, such as for example in the range of from 10 to 20, different polypeptides selected from the group of SEQ ID NO:1-51 or fragments thereof.

Vaccines comprising full-length polypeptides and/or fragments and/or variants

In preferred embodiments, the invention relates to a vaccine for prevention of infection with and/or development of disease from Campylobacter jejuni comprising any of the polypeptides of SEQ ID NO:1-51, such as any of SEQ ID NO:1-36 or any of SEQ ID NO:37-51, or a fragment or variant thereof. Preferred fragments and variants are those described in the sections herein that relate to fragments and variants.

Accordingly, in these embodiments, the antigenicity or immunogenicity is provided by direct administration of a polypeptide normally located on the surface of a Campylobacter jejuni cell. In one particular embodiment, the polypeptides are selected so that a vaccine comprises multiple polypeptides capable of associating with different MHC molecules, such as different MHC class I molecules. Preferably, a vaccine comprises polypeptides and/or fragments capable of associating with the most frequently occurring MHC class I molecules. In one particular embodiment of the Invention, the vaccine comprises one or more polypeptides and/or fragments

capable of associating to an MHC class I molecule and one or more polypeptides and/or fragments capable of associating with an MHC class II molecule. Hence, a vaccine is in some embodiments capable of raising a specific cytotoxic T-cells response and/or a specific helper T-cell response. Association to MHC molecules can e.g. be determined as described by Andersen et al. (1999) Tissue Antigens 54:185; or by Tan et al. (1997) J. Immunol. Methods 209:25.

Adjuvants and immunogenic carriers

Preferably, vaccines of the present invention comprise a pharmaceutically-acceptable carrier as described herein in the section 'Compositions of the invention'.

The vaccine can further comprise an adjuvant. Adjuvants are substances whose admixture into the vaccine composition increases or otherwise modifies the immune response to a polypeptide. Adjuvants could for example be any of: $AlK(SO_4)_2$, $AlNa(SO_4)_2$, $AlNH_4(SO_4)$, silica, alum, $Al(OH)_3$, $Ca_3(PO_4)_2$, kaolin, carbon, aluminium hydroxide, aluminium phosphate, muramyl dipeptides, N-acetyl-muramyl-L-threonyl-D-isoglutamine (thr-DMP), N-acetyl-nornuramyl-L-alanyl-D-isoglutamine (CGP 11687, also referred to as nor-MDP), N-acetylmuramyul-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'2'-dipalmitoyl-sn-glycero-3-hydroxphosphoryloxy)-ethylamine (CGP 19835A, also referred to as MTP-PE), RIBI (MPL+TDM+CWS) in a 2% squalene/Tween-80.RTM. emulsion, lipopolysaccharides and derivatives, including lipid A, Freund's Complete Adjuvant (FCA), Freund's Incomplete Adjuvants, Merck Adjuvant 65, polynucleotides (for example, poly IC and poly AU acids), wax D from Mycobacterium, tuberculosis, substances found in Corynebacterium parvum, Bordetella pertussis, and members of the genus Brucella, liposomes or other lipid emulsions, Titermax, ISCOMS, Quil A, ALUN (see US 58767 and 5,554,372), Lipid A derivatives, choleratoxin derivatives, HSP derivatives, LPS derivatives, synthetic peptide matrixes or GMDP, Interleukin 1, Interleukin 2, Montanide ISA-51 and QS-21. Preferred adjuvants to be used with the invention include Montanide ISA-51 and QS-21. Montanide ISA-51 (Seppic, Inc.) is a mineral oil-based adjuvant analogous to incomplete Freund's adjuvant, which must be administered as an emulsion. QS-21 (Antigenics; Aquila Biopharmaceuticals, Framingham, MA) is a highly purified, water-soluble saponin that handles as an aqueous solution.

Desirable functionalities of adjuvants capable of being used in accordance with the present invention are listed in the below table.

Table 1 Modes of adjuvant action

Action	Adjuvant type	Result
1. Immunomodulation	Generally small molecule or protein which exploits cytokine network	Upregulation of immune response. Selection of Th1 or Th2
2. Presentation	Co-entity or chemically associated with immunogen in its native conformation	Increased neutralising antibody response. Greater duration of response
3. CTL inducer	Particles which can bind or enclose immunogen and which can fuse with or destroy cell membrane(s) Site emulsions for direct attachment of peptide to cell surface MHC-1	Cytosolic processing of protein yielding correct class 1 restricted peptide(s) Simple process if continuous peptide(s) known
4. Targeting	Particulate adjuvants which bind immunogen. Adjuvants which activate scavenger cells Carbohydrate adjuvants which bind lectin receptors on macrophages and DCs Site emulsion for short term Microspheres or nanospheres for long term	Efficient use of antigen and immunogen As above. May also determine type of response if targeting selective Efficient Potential for single dose vaccine
5. Depot formation		

Source: **John C. Cox and Alan R. Coulter** Vaccine 1997 Feb;15(3):248-56

A vaccine composition according to the present invention may comprise more than one different adjuvant. It is also contemplated that the Campylobacter polypeptide of the invention, or one or more fragments thereof, and the adjuvant can be administered separately in any appropriate sequence.

Frequently, the adjuvant of choice is Freund's complete or incomplete adjuvant, or killed *B. pertussis* organisms, used e.g. in combination with alum precipitated antigen. A general discussion of adjuvants is provided in Goding, Monoclonal Antibodies: Principles & Practice (2nd edition, 1986) at pages 61-63. Goding notes, however, that when the antigen of interest is of low molecular weight, or is poorly immunogenic, coupling to an immunogenic carrier is recommended (see below). Various saponin extracts and cytokines have also been suggested to be useful as adjuvants in immunogenic compositions. Recently, it has been proposed to use granulocyte-macrophage colony stimulating factor (GM-CSF), a well known cytokine, as an adjuvant (WO 97/28816).

In addition, a vaccine of the invention can comprise an immunogenic carrier such as a scaffold structure, for example a protein or a polysaccharide, to which the Campylobacter polypeptide or the fragment thereof is capable of being associated. A Campylobacter polypeptide, or the fragment thereof, present in the vaccine composition can be associated with an immunogenic carrier such as e.g. a protein. The association of the polypeptide to a carrier protein may be covalent or non-covalent. An immunogenic carrier protein may be present independently of an adjuvant. The function of a carrier protein can for example be to increase the molecular weight of in particular fragments in order to increase their activity or immunogenicity, to confer stability, to increase the biological activity, or to increase serum half-life. Furthermore, an immunogenic carrier protein may aid presenting the

Campylobacter polypeptide or the fragments thereof to T-cells. A carrier protein could be, but is not limited to, keyhole limpet hemocyanin, serum proteins such as transferrin, bovine serum albumin, human serum albumin, thyroglobulin or ovalbumin, immunoglobulins, or hormones, such as insulin. Tetanus toxoid and/or diptheria toxoid are also suitable carriers in one embodiment of the invention. Alternatively or additionally, dextrans, for example sepharose may be added. In yet another embodiment, an antigen-presenting cell such as e.g. a dendritic cell capable of presenting the polypeptide or a fragment thereof to a T-cell may be added to obtain the same effect as a carrier protein.

Methods for the preparation of vaccines have e.g. been described in US 5,470,958 and references therein. An effective amount of the polypeptide component of a vaccine of the invention, if injected, will typically be in the range of from about 0.1 to about 1000 µg, such as e.g. from about 1 to about 900 µg, for example from about 5 to about 500 µg, for a human subject, and generally in the range of from about 0.01 to 10.0 µg/Kg body weight of a subject animal. The above-indicated ranges are merely indicative and should not be interpreted as limiting the present invention.

An effective amount of an antigenic polypeptide of the invention may be an amount capable of eliciting a detectable humoral immune response in the absence of an immunomodulator. For many immunogens, this is in the range of about 5-100 µg for a human subject. The appropriate amount of immunogen to be used is dependent on the immunological response it is desired to elicit. Furthermore, the exact effective amount necessary will vary from subject to subject, depending on the species, age and general condition of the subject, the severity of the condition being treated, the mode of administration, etc. It is therefore not always possible to specify an exact effective amount. However, the appropriate effective amount may be determined by one of ordinary skill in the art using only routine experimentation or prior knowledge in the art.

<u>DNA vaccines and vaccines comprising recombinant viruses or recombinant cells</u>

DNA or RNA vaccines pertain to the introduction of e.g. an antigenic polypeptide determinant into a patient by overexpressing in the cells of the patient a polynucleotide construct which includes expression control sequences operably linked to a

sequence encoding the polypeptide of interest, herein a polypeptide of any of SEQ ID NO:1-51 or a variant or fragment thereof. As such fragments may not contain a methionine start codon, such a codon is optionally included as part of the expression control sequences. The polynucleotide construct may be a non-replicating and linear polynucleotide, a circular expression vector, or an autonomously replicating plasmid or viral expression vector. The construct may become integrated into the host genome. Any expression vector that can transfect a mammalian cell may be used in the methods of immunising an individual according to the present invention. Methods for constructing expression vectors are well known in the art (see, e.g., Molecular Cloning: A Laboratory Manual, Sambrook et al., eds., Cold Spring Harbor Laboratory, 2nd Edition, Cold Spring Harbor, N.Y., 1989). Preferred are vaccines comprising a plurality of genes expressing multiple polypeptides selected from SEQ ID NO:1-51 and/or multiple fragments of the invention, thereby permitting simultaneous vaccination against a variety of preselected targets.

Vaccines can also be prepared by incorporating a polynucleotide encoding a specific antigenic polypeptide of interest into a living but harmless vector, such as a virus or a cell, such as an attenuated or reduced-virulence E. coli or Salmonella cell. The harmless recombinant virus or recombinant cell is injected into the intended recipient. Such a recombinant cell may be dead or alive. If alive, the recombinant organism may replicate in the host while producing and presenting the antigenic polypeptide to the host's immune system. It is contemplated that this type of vaccine will be more effective than the non-replicative type of vaccine. For such a vaccine to be successful, the vector organism must be viable, and either be naturally non-virulent or have an attenuated or reduced-virulence phenotype.

Strategies for vaccination using attenuated bacteria and suitable bacterial strains for use therein have been described in e.g. Makino et al. (2001) Microb. Pathog. 31:1-8; Gentschev et al. (2002) Int. J. Med. Microbiol. 291:577-582; Turner et al. (2001) Infect. Immun. 69:4969-4979; WO99/49026; and WO03/022307.

Further examples of vectors that can be applied are vectors comprising e.g., retroviruses, as disclosed in WO 90/07936, WO 91/02805, WO 93/25234, WO 93/25698, and WO 94/03622, adenovirus, as disclosed by Berkner, Biotechniques 6:616-627, 1988; Li et al., Hum. Gene Ther. 4:403-409, 1993; Vincent et al., Nat. Genet. 5:130-134, 1993; and Kolls et al., Proc. Natl. Acad. Sci. USA 91:215-219, 1994), pox virus, as disclosed by U.S. 4,769,330; U.S. Pat. No. 5,017,487; and WO 89/01973, naked DNA as disclosed WO 90/11092, a polynucleotide molecule com-

plexed to a polycationic molecule as disclosed in WO 93/03709, and polynucleotides associated with liposomes as disclosed by Wang et al., Proc. Natl. Acad. Sci. USA 84:7851, 1987. In certain embodiments, the DNA may be linked to killed or inactivated adenovirus as disclosed by Curiel et al., Hum. Gene Ther. 3:147-154, 1992; Cotton et al., Proc. Natl. Acad. Sci. USA 89:6094, 1992. Other suitable compositions include DNA-ligands as disclosed by Wu et al., J. Biol. Chem. 264:16985-16987, 1989), and lipid-DNA combinations as disclosed by Felgner et al., Proc. Natl. Acad. Sci. USA 84:7413-7417, 1989). In addition, the efficiency of naked DNA uptake into cells may be increased by coating the DNA onto biodegradable latex beads.

Vaccine vectors preferably comprise a suitable promoter which is operably linked to the polynucleotide sequence encoding the immunogenic polypeptide. Any promoter that can direct a high level of transcription initiation in the target cells may be used in the invention. Non-tissue specific promoters, such as the cytomegalovirus (DeBernardi et al., Proc Natl Acad Sci USA 88:9257-9261 [1991], and references therein), mouse metallothionine I (Hammer et al., J Mol Appl Gen 1:273-288 [1982]), HSV thymidine kinase (McKnight, Cell 31:355-365 [1982]), and SV40 early (Benoist et al., Nature 290:304-310 [1981]) promoters may thus also be used.

Methods of vaccination

In a further main aspect, the present invention relates to the use of any one or more of

- a polypeptide which comprises any of the sequences of SEQ ID NO:1-51, such as any of SEQ ID NO:1-36 or any of SEQ ID NO:37-51; or comprises a fragment or variant of any of said sequences,
- a polynucleotide comprising a sequence encoding said polypeptide,
- an expression vector comprising a sequence encoding said polypeptide,
- a recombinant virus or recombinant cell comprising said polynucleotide or said expression vector,

or

- a composition as defined herein,

for the preparation of a medicament for the immunisation of an animal or human being against Campylobacter jejuni infections.

Similarly, the invention relates to a method for the immunisation of an animal or human being against a Campylobacter jejuni infections comprising the step of administering any one or more of

- a polypeptide which comprises any of the sequences of SEQ ID NO:1-51, such as any of SEQ ID NO:1-36 or any of SEQ ID NO:37-51; or comprises a fragment or variant of any of said sequences,
- a polynucleotide comprising a sequence encoding said polypeptide,
- an expression vector comprising a sequence encoding said polypeptide,
- a recombinant virus or recombinant cell comprising said polynucleotide or said expression vector,

  or
- a composition as defined herein.

The animal may be any bird or mammal, e.g. a chicken, duck, turkey, cow or pig.. Particular target populations of human beings may be individuals from at-risk populations, such as the population of children up to 4 years old, the population of persons in industrialised nations or the population of naive or semi-immune travellers to the developing world.

Modes of administration of the composition according to the invention include, but are not limited to systemic administration, such as intravenous or subcutaneous administration, intradermal administration, intramuscular administration, intranasal administration, oral administration, and generally any form of mucosal administration.

The immunogenic effect according to the present invention can e.g. be measured by assay of antibodies in serum samples e.g. by a RIA. Furthermore, the effect can be determined in vivo, by measuring e.g. an increased T cell responsiveness to T cell dependent antigenic polypeptides, wherein said increased responsiveness is characteristic of an enhancement of a normal immune response to such antigenic polypeptides. An immunostimulating effect may also be measured as an enhanced T cell production of, in particular, IL-2, IL-3, IFN-γ and/or GM-CSF. Polypeptides or fragments thereof having a potential for eliciting an enhanced immune response may thus be readily identified by screening for enhanced IL-2, IL-3, IFN-γ or GM-CSF production by T cells, as described e.g. in US 07/779,499, incorporated herein by reference. Young et al. (2000) In: Campylobacter, 2nd ed. Ed. by Nachamkin and

Blaser, American Society for Microbiology, pp. 287-301 also describe a series of suitable animal models which can be of use in the evaluation of the efficacy of therapeutic and preventive strategies and compositions. A number of aspects related to vaccination against Campylobacter, including potential target populations, animal models and vaccination strategies have been described by Scott and Tribble (2000) In: Campylobacter, 2nd ed. Ed. by Nachamkin and Blaser, American Society for Microbiology, pp. 303-319).

The herein described polynucleotides and expression vectors can be introduced into target cells in vivo or in vitro by any standard method: e.g., as naked DNA (Donnelly et al., Annu Rev Immunol 15:617-648 [1997]), incorporated into ISCOMS, liposomes, or erythrocyte ghosts, or by biolistic transfer, calcium precipitation, or electroporation. Alternatively, one can employ a viral-based vector as a means for introducing the polynucleotide encoding the polypeptide of interest into the cells of the animal or human being. Preferred viral vectors include those derived from replication-defective hepatitis viruses (e.g., HBV and HCV), retroviruses (see, e.g., WO89/07136; and Rosenberg et al., N Eng J Med 323 (9):570-578 [1990]), adenovirus (see, e.g., Morsey et al., J Cell Biochem, Supp. 17E [1993]), adeno-associated virus (Kotin et al., Proc Natl Acad Sci USA 87:2211-2215 [1990]), replication defective herpes simplex viruses (HSV; Lu et al., Abstract, page 66, Abstracts of the Meeting on Gene Therapy, Sep. 22-26, 1992, Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.), canary pox virus, and any modified versions of these vectors. Cells transfected in vitro can be cultured and cloned, if desired, prior to introduction into the patient.

In addition to direct in vivo procedures, ex vivo procedures may be used in which cells are removed from an animal, modified, and placed into the same or another animal. It will be evident that one can utilise any of the compositions noted above for introduction of an antigenic polypeptides or polynucleotides encoding such according to the invention into tissue cells in an ex vivo context. Protocols for viral, physical and chemical methods of uptake are well known in the art. Thus, as an alternative to administration of a polypeptide of the invention or a vector capable of expressing such a polypeptide directly to the patient, one can remove helper T cells from the patient; stimulate those T cells ex vivo using the same antigenic polypeptide or vector; and introduce the stimulated helper T cells into the same patient.

Antibodi s and methods for raising antibodi s of the invention

In a further main aspect, the invention relates to antibodies capable of specifically (recognising and) binding any of the polypeptides of SEQ ID NO:1-36 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:1 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:2 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:3 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:4 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:5 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:6 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:7 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:8 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:9 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:10 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:11 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:12 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:13 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:14 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:15 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:16 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:17 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:18 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:19 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:20 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:21 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:22 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:23 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:24 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:25 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:26 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:27 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:28 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:29 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:30 and/or

a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:31 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:32 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:33 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:34 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:35 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:36 and/or a fragment and/or a variant thereof.

In preferred embodiments, the antibodies of the invention are capable of specifically of binding an intact Campylobacter jejuni cell, i.e. capable of binding a living or a dead Campylobacter cell which has maintained its structural integrity, preferably a cell that has maintained the integrity of the outer membrane (i.e. wherein the outer membrane is not permeabilised). Binding of antibodies to intact cells can e.g. be determined by flow cytometry as described in Rioux et al.(2001) Infect. Immun. 69:5162-5165 or as described in Singh et al. (2003) Infect. Immun. 71:3937-3946.

In another main aspect, the invention relates to an antibody capable of specifically (recognising and) binding an intact Campylobacter jejuni cell and capable of specifically binding any of the polypeptides of SEQ ID NO:37-51 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:37 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:38 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:39 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:40 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:41 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:42 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:43 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:44 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:45 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:46 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:47 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:48 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:49 and/or a fragment and/or a variant thereof, for example the polypeptide of SEQ ID NO:50 and/or a fragment and/or a variant thereof, such as the polypeptide of SEQ ID NO:51 and/or a fragment and/or a variant thereof.

Preferred antibodies are ones that specifically bind with a dissociation constant or Kd less than 5 X 10^{-6}M, such as less than 10^{-6}M, e.g. less than 5 X 10^{-7}M, such as less than 10^{-7}M, e.g. less than 5 X 10^{-8}M, such as less than 10^{-8}M, e.g. less than 5 X 10^{-9}M, such as less than 10^{-9}M, e.g. less than 5 X 10^{-10}M, such as less than 10^{-10}M, e.g. less than 5 X 10^{-11}M, such as less than 10^{-11}M, e.g. less than 5 X 10^{-12}M, such as less than 10^{-12}M, e.g. less than 5 X 10^{-13}M, such as less than 10^{-13}M, e.g. less than 5 X 10^{-14}M, such as less than 10^{-14}M, e.g. less than 5 X 10^{-15}M, or less than 10^{-15}M. Binding constants can be determined using methods well-known in the art, such as ELISA (e.g. as described in Orosz and Ovadi (2002) J. Immunol. Methods 270:155-162) or surface plasmon resonance analysis.

Antibodies can be used for passive immunisation of mammals, preferably human beings, more preferably immunocompromised patients. A treatment with antibodies can be done to cure or to prevent Campylobacter jejuni infections.

Antibodies of the invention may be mechanistically divided into the following preferred groups:

1. Function-inhibiting antibodies that work as an antibacterial (affect the viability of the bacterium). Such antibodies should be effective regardless of the immune status of the patient. Preferably, such antibodies are capable of reducing Campylobacter jejuni growth in vitro to less than 50%, such as less than 25%, for example less than 10%, such as less than 5% of a control without antibody added.
2. Opsonising antibodies that are designed to enhance phagocytic killing. Effectiveness of such antibodies may depend on the immune status of the patient, but it is very well possible that they will enhance phagocytic killing even in compromised patients.
3. Antibodies conjugated to a therapeutic moiety such as a toxin or bactericidal agent, e g. ricin or radioisotopes. Techniques for conjugating a therapeutic moiety to antibodies are well known, see, e.g. Thorpe et al.(1982) Immunol. Rev. 62, 119-158. These antibodies should also be effective regardless of the immune status of the patient.

An antibody with or without a therapeutic moiety conjugated to it can be used as a therapeutic that is administered alone or in combination with chemotherapeutics or other therapeutic agents.

In a further main aspect, the invention relates to a method for raising specific antibodies to a polypeptide of any of SEQ ID NO:1-36 in an (non-human) animal comprising the steps of

a. providing
   - a polypeptide comprising any of the sequences of SEQ ID NO:1-36, or comprising a fragment or variant thereof,
   - a polynucleotide comprising a sequence encoding said polypeptide,
   - an expression vector comprising a sequence encoding said polypeptide, or
   - a recombinant virus or recombinant cell of the invention as defined herein,
b. introducing a composition comprising said polypeptide, polynucleotide, vector or recombinant virus or recombinant cell into said animal,
c. raising antibodies in said animal, and
d. isolating and optionally purifying the antibodies.

A method for raising specific antibodies to a polypeptide of any of SEQ ID NO:37-51 in an (non-human) animal wherein the antibodies are capable of specifically binding an intact Campylobacter jejuni cell, the method comprising the steps of

a. providing
   - a polypeptide comprising any of the sequences of SEQ ID NO:37-51, or comprising a fragment or variant thereof,
   - a polynucleotide comprising a sequence encoding said polypeptide,
   - an expression vector comprising a sequence encoding said polypeptide, or
   - a recombinant Escherichia coli or Salmonella cell of the invention as defined herein,
b. introducing a composition comprising said polypeptide, polynucleotide, vector or recombinant virus or recombinant cell into said animal,
c. raising antibodies in said animal,
d. isolating and optionally purifying the antibodies, and
e. selecting antibodies capable of specifically binding an intact Campylobacter jejuni cell.

The above methods are preferably done in a transgenic animal which can produce human antibodies.

Monoclonal/polyclonal antibodies

Antibodies of the invention may be polyclonal antibodies or monoclonal antibodies or mixtures of monoclonal antibodies. In a preferred embodiment, the antibody is a monoclonal antibody or a fragment thereof. Monoclonal antibodies (Mab's) are antibodies wherein every antibody molecule is similar and thus recognises the same epitope. The antibody may be any kind of antibody, however, it is preferably an IgG or IgA antibody.

Monoclonal antibodies are in general produced by a hybridoma cell line. Methods of making monoclonal antibodies and antibody-synthesising hybridoma cells are well known to those skilled in the art. Antibody-producing hybridomas may for example be prepared by fusion of an antibody-producing B lymphocyte with an immortalised cell line. A monoclonal antibody can be produced by the following steps. An animal is immunised with an antigen such as a full-length polypeptide or a fragment thereof. The immunisation is typically accomplished by administering the antigen to an immunologically competent mammal in an immunologically effective amount, i.e., an amount sufficient to produce an immune response. Preferably, the mammal is a rodent such as a rabbit, rat or mouse. The mammal is then maintained on a booster schedule for a time period sufficient for the mammal to generate high affinity antibody molecules. A suspension of antibody-producing cells is removed from each immunised mammal secreting the desired antibody. After a sufficient time to generate high affinity antibodies, the animal (e.g. mouse) is sacrificed and antibody-producing lymphocytes are obtained from one or more of the lymph nodes, spleens and peripheral blood. Spleen cells are preferred, and can be mechanically separated into individual cells in a physiological medium using methods well known to one of skill in the art. The antibody-producing cells are immortalised by fusion to cells of a mouse myeloma line. Mouse lymphocytes give a high percentage of stable fusions with mouse homologous myelomas, however, rat, rabbit and frog somatic cells can also be used. Spleen cells of the desired antibody-producing animals are immortalised by fusing with myeloma cells, generally in the presence of a fusing agent such as polyethylene glycol. Any of a number of myeloma cell lines suitable as a fusion partner can be, for example, the P3-NS1/1-Ag4-1, P3-x63-Ag8.653 or Sp2/O-Ag14 myeloma lines, available from the American Type Culture Collection (ATCC), Rockville, Md.

Monoclonal antibodies can also be generated by other methods well known to those skilled in the art of recombinant DNA technology. An alternative method,

referred to as the "combinatorial antibody display" method, has been developed to identify and isolate antibody fragments having a particular specificity, and can be utilised to produce monoclonal antibodies.

A polyclonal antibody is a mixture of antibody molecules recognising a specific given antigen, hence polyclonal antibodies may recognise different epitopes within e.g. a polypeptide. In general polyclonal antibodies are purified from serum of a mammal, which previously has been immunised with the antigen. Polyclonal antibodies may for example be prepared by any of the methods described in Antibodies: A Laboratory Manual, By Ed Harlow and David Lane, *Cold Spring Harbor Laboratory Press, 1988.* Polyclonal antibodies may be derived from any suitable mammalian species, for example from mice, rats, rabbits, donkeys, goats, and sheep.

Specificity

The antibodies of the invention may be monospecific towards any of the polypeptides of SEQ ID NO:1-51. In another embodiment, the antibody is bispecific or multispecific having at least one portion being specific towards any of the polypeptides of SEQ ID NO:1-51.

Monospecific antibodies may be monovalent, i.e. having only one binding domain. For a monovalent antibody, the immunoglobulin constant domain amino-acid sequences preferably comprise the structural portions of an antibody molecule known in the art as CH1, CH2, CH3 and CH4. Preferred are those which are known in the art as C_L. Furthermore, insofar as the constant domain can be either a heavy or light chain constant domain (C_H or C_L, respectively), a variety of monovalent antibody compositions are contemplated by the present invention. For example, light chain constant domains are capable of disulphide bridging to either another light chain constant domain, or to a heavy chain constant domain. In contrast, a heavy chain constant domain can form two independent disulphide bridges, allowing for the possibility of bridging to both another heavy chain and to a light chain, or to form polymers of heavy chains. Thus, in another embodiment, the invention contemplates a composition comprising a monovalent polypeptide wherein the constant chain domain C has a cysteine residue capable of forming at least one disulphide bridge, and where the composition comprises at least two monovalent polypeptides covalently linked by said disulphide bridge.

In another embodiment of the invention the antibody is a multivalent antibody having at least two binding domains. The binding domains may have specificity for the same ligand or for different ligands.

Multispecificity, including bispecificity

In a preferred embodiment the invention relates to multispecific antibodies, which have affinity for and are capable of specifically binding at least two different entities.

In one embodiment, the multispecific antibody is a bispecific antibody, which carries at least two different binding domains, at least one of which is of antibody origin. A bispecific molecule of the invention can also be a single chain bispecific molecule. Multispecific molecules can also be single-chain molecules or may comprise at least two single-chain molecules. The multispecific, including bispecific antibodies, may be produced by any suitable manner known to the person skilled in the art. A number of approaches have been developed such as the ones described in WO 94/09131; WO 94/13804; WO 94/13806 or U.S. Pat. Nos. 5,260,203; 5,455,030; 4,881,175; 5,132,405; 5,091,513; 5,476,786; 5,013,653; 5,258,498; and 5,482,858.

Using a bispecific or multispecific antibody according to the invention the invention offers several advantages as compared to monospecific/monovalent antibodies. A bispecific/multispecific antibody has a first binding domain capable of specifically recognising and binding any of the Campylobacter jejuni polypeptides of SEQ ID NO:1-51, whereas the other binding domain(s) may be used for other purposes. In one embodiment, at least one other binding domain is used for binding to a Campylobacter jejuni polypeptide, such as binding to another epitope on the same Campylobacter jejuni polypeptide as the first binding domain. Thereby specificity for Campylobacter jejuni may be increased as well as increase of avidity of the antibody. In another embodiment the at least one other binding domain may be used for specifically binding a mammalian cell, such as a human cell. It is preferred that the at least other binding domain is capable of binding an immunoactive cell, such as a leukocyte, a macrophage, a lymphocyte, a basophilic cell, and/or an eosinophilic cell, in order to increase the effect of the antibody in a therapeutic method. This may be accomplished by establishing that the at least one other binding domain is capable of specifically binding a mammalian protein, such as a human protein, such as a protein selected from any of the cluster differentiation proteins (CD), in particular CD64 and/or CD89..

Humanised antibodies

It is not always desirable to use non-human antibodies for human therapy, since the non-human "foreign" epitopes may elicit an immune response in the individual to be treated. To eliminate or minimise the problems associated with non-human antibodies, it is desirable to engineer chimeric antibody derivatives, i.e., "humanised" antibody molecules that combine the non-human Fab variable region binding determinants with a human constant region (Fc). Such antibodies are characterised by equivalent antigen specificity and affinity of the monoclonal and polyclonal antibodies described above, and are less immunogenic when administered to humans, and therefore more likely to be tolerated by the individual to be treated.

Accordingly, in one embodiment the antibody of the invention is a humanised antibody. Humanised antibodies are in general chimeric antibodies comprising regions derived from a human antibody and regions derived from a non-human antibody, such as a rodent antibody. Humanisation (also called Reshaping or CDR-grafting) is a well-established technique for reducing the immunogenicity of monoclonal antibodies (mAbs) from xenogeneic sources (commonly rodent), increasing the homology to a human immunoglobulin, and for improving their activation of the human immune system. Thus, humanised antibodies are typically human antibodies in which some CDR residues and possibly some framework residues are substituted by residues from analogous sites in rodent antibodies.

It is important that humanised antibodies retain high affinity for the antigen and other favourable biological properties. To achieve this goal, according to a preferred method, humanised antibodies are prepared by a process of analysis of the parental sequences and various conceptual humanised products using three-dimensional models of the parental and humanised sequences. Three-dimensional immunoglobulin models are commonly available and are familiar to those skilled in the art. Computer programs are available which illustrate and display probable three-dimensional conformational structures of selected candidate immunoglobulin sequences. Inspection of these displays permits analysis of the likely role of certain residues in the functioning of the candidate immunoglobulin sequence, i.e., the analysis of residues that influence the ability of the candidate immunoglobulin to bind its antigen. In this way, FR residues can be selected and combined from the recipient and import sequences so that the desired antibody characteristic, such as

increased affinity for the target antigen(s), is maximised, although it is the CDR residues that directly and most substantially influence antigen binding.

One method for humanising MAbs relates to production of chimeric antibodies in which an antigen binding site comprising the complete variable domains of one antibody is fused to constant domains derived from a second antibody, preferably a human antibody. Methods for carrying out such chimerisation procedures are for example described in EP-A-0 120 694 (Celltech Limited), EP-A-0 125 023 (Genentech Inc.), EP-A-0 171 496 (Res. Dev. Corp. Japan), EP-A-0173494 (Stanford University) and EP-A-0 194 276 (Celltech Limited).

The humanised antibody of the present invention may be made by any method capable of replacing at least a portion of a CDR of a human antibody with a CDR derived from a non-human antibody. Winter describes a method which may be used to prepare the humanised antibodies of the present invention (UK Patent Application GB 2188638A), the contents of which are incorporated by reference.

As an example, the humanised antibodies of the present invention may be produced by the following process:

(a) constructing, by conventional techniques, an expression vector containing an operon with a DNA sequence encoding an antibody heavy chain in which the CDRs and such minimal portions of the variable domain framework region that are required to retain antibody binding specificity are derived from a non-human immunoglobulin, and the remaining parts of the antibody chain are derived from a human immunoglobulin;

(b) constructing, by conventional techniques, an expression vector containing an operon with a DNA sequence encoding a complementary antibody light chain in which the CDRs and such minimal portions of the variable domain framework region that are required to retain donor antibody binding specificity are derived from a non-human immunoglobulin, and the remaining parts of the antibody chain are derived from a human immunoglobulin;

(c) transfecting the expression vectors into a host cell by conventional techniques; and

(d) culturing the transfected cell by conventional techniques to produce the humanised antibody.

The host cell may be co-transfected with the two vectors of the invention, the first vector containing an operon encoding a light chain derived polypeptide and the sec-

ond vector containing an operon encoding a heavy chain derived polypeptide. The two vectors contain different selectable markers, but otherwise, apart from the antibody heavy and light chain coding sequences, are preferably identical, to ensure, as far as possible, equal expression of the heavy and light chain polypeptides. Alternatively, a single vector may be used, the vector including the sequences encoding both the light and the heavy chain polypeptides. The coding sequences for the light and heavy chains may comprise cDNA or genomic DNA or both.

The host cell used to express the altered antibody of the invention may be either a bacterial cell such as Escherichia coli, or a eukaryotic cell. In particular a mammalian cell of a well defined type for this purpose, such as a myeloma cell or a Chinese hamster ovary cell may be used.

The general methods by which the vectors of the invention may be constructed, transfection methods required to produce the host cell of the invention and culture methods required to produce the antibody of the invention from such host cells are all conventional techniques. Likewise, once produced, the humanised antibodies of the invention may be purified according to standard procedures.

Human antibodies

In a more preferred embodiment the invention relates to an antibody, wherein the binding domain is carried by a human antibody, i.e. wherein the antibodies have a greater degree of human peptide sequences than do humanised antibodies.

Human mAb antibodies directed against human proteins can be generated using transgenic mice carrying the human immune system rather than the mouse system. Splenocytes from these transgenic mice immunised with the antigen of interest are used to produce hybridomas that secrete human mAbs with specific affinities for epitopes from a human protein (see, e.g., Wood et al. International Application WO 91/00906, Kucherlapati et al. PCT publication WO 91/10741; Lonberg et al. International Application WO 92/03918; Kay et al. International Application 92/03917; Lonberg, N. et al. 1994 Nature 368:856-859; Green, L. L. et al. 1994 Nature Genet. 7:13-21; Morrison, S. L. et al. 1994 Proc. Natl. Acad. Sci. USA 81:6851-6855; Bruggeman et al. 1993 Year Immunol 7:33-40; Tuaillon et al. 1993 PNAS 90:3720-3724; Bruggeman et al. 1991 Eur J Immunol 21:1323-1326). Such transgenic mice are available from Abgenix, Inc., Fremont, Calif., and Medarex, Inc., Annandale, N.J. It has been described that the homozygous deletion of the antibody heavy-chain joining region (IH) gene in chimeric and germ-line mutant mice results

in complete inhibition of endogenous antibody production. Transfer of the human germ-line immunoglobulin gene array in such germ-line mutant mice will result in the production of human antibodies upon antigen challenge. See, e.g., Jakobovits et al., Proc. Natl. Acad. Sci. USA 90:2551 (1993); Jakobovits et al., Nature 362:255-258 (1993); Bruggemann et al., Year in Immunol. 7:33 (1993); and Duchosal et al. Nature 355:258 (1992). Human antibodies can also be derived from phage-display libraries (Hoogenboom et al ., J. Mol. Biol. 227: 381 (1992); Marks et al., J. Mol. Biol. 222:581-597 (1991); Vaughan, et al., Nature Biotech 14:309 (1996)).

Suitable methods for producing human monoclonal antibodies have furthermore been described in WO 03/017935, WO 02/100348, US 2003 091561, and US 2003 194403

Binding fragments of antibodies

In one embodiment of the invention, the antibody is a fragment of an antibody, preferably an antigen binding fragment or a variable region. Examples of antibody fragments useful with the present invention include Fab, Fab', $F(ab')_2$ and Fv fragments. Papain digestion of antibodies produces two identical antigen binding fragments, called the Fab fragment, each with a single antigen binding site, and a residual "Fc" fragment, so-called for its ability to crystallise readily. Pepsin treatment yields an $F(ab')_2$ fragment that has two antigen binding fragments which are capable of cross-linking antigen, and a residual other fragment (which is termed pFc'). Additional fragments can include diabodies, linear antibodies, single-chain antibody molecules, and multispecific antibodies formed from antibody fragments.

The antibody fragments Fab, Fv and scFv differ from whole antibodies in that the antibody fragments carry only a single antigen-binding site. Recombinant fragments with two binding sites have been made in several ways, for example, by chemical cross-linking of cysteine residues introduced at the C-terminus of the VH of an Fv (Cumber et al., 1992), or at the C-terminus of the VL of an scFv (Pack and Pluckthun, 1992), or through the hinge cysteine residues of Fab's (Carter et al., 1992).

Preferred antibody fragments retain some or essentially all of the ability of an antibody to selectively binding with its antigen. Some preferred fragments are defined as follows:

(1) Fab is the fragment that contains a monovalent antigen-binding fragment of an antibody molecule. A Fab fragment can be produced by digestion of whole anti-

body with the enzyme papain to yield an intact light chain and a portion of one heavy chain.

(2) Fab' is the fragment of an antibody molecule and can be obtained by treating whole antibody with pepsin, followed by reduction, to yield an intact light chain and a portion of the heavy chain. Two Fab' fragments are obtained per antibody molecule. Fab' fragments differ from Fab fragments by the addition of a few residues at the carboxyl terminus of the heavy chain CH1 domain including one or more cysteines from the antibody hinge region.

(3) $(Fab')_2$ is the fragment of an antibody that can be obtained by treating whole antibody with the enzyme pepsin without subsequent reduction. $F(ab')_2$ is a dimer of two Fab' fragments held together by two disulfide bonds.

(4) Fv is the minimum antibody fragment that contains a complete antigen recognition and binding site. This region consists of a dimer of one heavy and one light chain variable domain in a tight, non-covalent association (V_H -V_L dimer). It is in this configuration that the three CDRs of each variable domain interact to define an antigen binding site on the surface of the V_H -V_L dimer. Collectively, the six CDRs confer antigen binding specificity to the antibody. However, even a single variable domain (or half of an Fv comprising only three CDRs specific for an antigen) has the ability to recognise and bind antigen, although at a lower affinity than the entire binding site.

In one embodiment of the present invention the antibody is a single-chain antibody, defined as a genetically engineered molecule containing the variable region of the light chain, the variable region of the heavy chain, linked by a suitable polypeptide linker as a genetically fused single chain molecule. Such single-chain antibodies are also referred to as "single-chain Fv" or "sFv" antibody fragments. Generally, the Fv polypeptide further comprises a polypeptide linker between the V_H and V_L domains that enables the sFv to form the desired structure for antigen binding.

The antibody fragments according to the invention may be produced in any suitable manner known to the person skilled in the art. Several microbial expression systems have already been developed for producing active antibody fragments, e.g. the production of Fab in various hosts, such as E. coli or yeast has been described. The fragments can be produced as Fab's or as Fv's, but additionally it has been shown that a V_H and a V_L can be genetically linked in either order by a flexible polypeptide linker, which combination is known as an scFv.

Compositions of th inv ntion

In a further aspect, the invention relates to a composition comprising a carrier and an isolated polypeptide consisting of any of the sequences set forth in SEQ ID NO:1-51, such as any of SEQ ID NO:1-36 or any of SEQ ID NO:37-51.

In a even further aspect, the invention relates to a composition comprising a carrier and any one or more of

- an antibody of the invention as defined herein,
- an antigenic fragment of the invention as defined herein,
- a polynucleotide of the invention as defined herein,
- an expression vector of the invention as defined herein,

  or
- a recombinant cell of the invention as defined herein.

In one embodiment, the carrier of the above compositions is water.

In a further main aspect, the present invention relates to pharmaceutical compositions useful for practising the methods described herein. Thus, the invention relates to a pharmaceutical composition comprising a pharmaceutically-acceptable carrier and

- an isolated polypeptide which comprises any of the sequences of SEQ ID NO:1-36, or comprises a fragment or variant of any of said sequences,
- an isolated polynucleotide comprising a sequence encoding said polypeptide,
- an expression vector comprising a sequence encoding said polypeptide,

  or
- a recombinant virus or recombinant cell comprising said polynucleotide or said expression vector.

Furthermore, the invention relates to a pharmaceutical composition comprising an antibody of the invention as defined herein and a pharmaceutically-acceptable carrier.

Pharmaceutical compositions of the present invention contain a pharmaceutically-acceptable carrier together with at least one species of polypeptide (incl. fragment and/or variant), antibody, polynucleotide, expression vector, or recombinant virus or recombinant cell as described herein, dissolved or dispersed therein as

an active ingredient. In one aspect, the invention relates to a pharmaceutical composition comprising at least one species as defined above. In other preferred embodiments, the pharmaceutical composition comprises at least two different species as defined above in order to increase the effect of the treatment.

As used herein, the term "pharmaceutically acceptable" used in connection with compositions or carriers represents that the materials are capable of being administered to or upon a human or animal without the production of undesirable physiological effects such as nausea, dizziness, gastric upset and the like.

The preparation of a pharmacological composition that contains active ingredients dissolved or dispersed therein is well understood in the art. Often such compositions are prepared as sterile injectables either as liquid solutions or suspensions, aqueous or non-aqueous, however, solid forms suitable for solution, or suspension, in liquid prior to use can also be prepared. The preparation can also be. emulsified. The active ingredient can be mixed with carriers which are pharmaceutically acceptable and compatible with the active ingredient and in amounts suitable for use in the methods described herein. Suitable carriers are, for example, water, saline, dextrose, glycerol, ethanol or the like and combinations thereof. In addition, if desired, the composition can contain minor amounts of auxiliary substances such as wetting or emulsifying agents, pH buffering agents and the like which enhance the effectiveness of the active ingredient.

The pharmaceutical composition of the present invention can include pharmaceutically-acceptable salts of the components therein. Pharmaceutically acceptable salts include the acid addition salts (formed with the free amino groups of the polypeptide) that are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids as acetic, tartaric, mandelic and the like. Salts formed with the free carboxyl groups can also be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, 2-ethylamino ethanol, histidine, procaine and the like.

Pharmaceutically-acceptable carriers are well known in the art. Exemplary of liquid carriers are sterile aqueous solutions that contain no materials in addition to the active ingredients and water, or contain a buffer such as sodium phosphate at physiological pH value, physiological saline or both, such as phosphate-buffered saline. Still further, aqueous carriers can contain more than one buffer salt, as well as salts such as sodium and potassium chlorides, dextrose, propylene glycol, poly-

ethylene glycol and other solutes. Liquid compositions can also contain liquid phases in addition to and to the exclusion of water. Exemplary of such additional liquid phases are glycerin, vegetable oils such as cottonseed oil, organic esters such as ethyl oleate, and water-oil emulsions.

A pharmaceutical composition containing a polypeptide or antibody of the present invention preferably contains an amount of at least 0.1 weight percent of polypeptide or antibody per weight of total pharmaceutical composition. A weight percent is a ratio by weight of polypeptide or antibody to total composition. Thus, for example, 0.1 weight percent is 0.1 grams of polypeptide or antibody per 100 grams of total composition.

The pharmaceutical composition may also be a kit-in-part further including an antibiotic agent, such as antibiotics selected from β-lactams, cephalosporins, penicilins, aminoglycosides, macrolide antibiotics (erythromycin, clarithromycin, or azithromycin) and fluoroquinolone antibiotics (ciprofloxacin, levofloxacin, gatifloxacin, or moxifloxacin) and/or including an immunostimulating agent, such as cytokines, interferons, growth factors, for example GCSF or GM-CSF. The kit-in-part may be used for simultaneous, sequential or separate administration.

Polypeptides of the invention

Fragments of the invention

In a main aspect, the invention relates to a fragment, preferably an antigenic fragment, of a polypeptide set forth in any of SEQ ID NO:1-51, such as a fragment of any of SEQ ID NO:1-36 or a fragment of any of SEQ ID NO:37-51. The length of such fragments may vary from 2 consecutive amino-acid residues of a polypeptide to the full-length polypeptide minus one amino-acid residue. Preferably, fragments are less than 100 consecutive amino acids, such as less than 70 or 50 consecutive amino acids, e.g. less than consecutive 40 amino acids, such as less than 30 consecutive amino acids, e.g. less than 25 consecutive amino acids, such as less than consecutive 20 amino acids in length. Thus, for example fragments can be 2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19 or 20 consecutive amino acids in length. In further preferred embodiments, a fragment comprises 6 or more, such as 7 or more, e.g. 8 or more, such as 9 or more, e.g. 10 or more consecutive amino acids of the corresponding full-length sequence. Preferred ranges include fragments of between 5 and 50 consecutive amino acids in length, such as between 5 and 25 consecutive amino acids in length, e.g. between 5 and 20 consecutive amino acids

in length. Expressed in another way, a fragment consists of a part of an amino-acid sequence which is less than 100% in length as compared to the full-length polypeptide. Preferably, the length of the fragment is less than 99%, such as less than 75%, e.g. less than 50%, such as less than 25%, e.g. less than 20%, such as less than 15%, e.g. less than 10% of the length of the full-length polypeptide. In further preferred embodiments, the fragment consists of a part of an amino-acid sequence which is less than 100%, but more than 1% in length as compared to the full-length polypeptide, such as less than 100% but more than 5%, e.g. less than 100% but more than 10%, such as less than 100% but more than 20%, e.g. less than 100% but more than 25%, such as less than 100% but more than 50% of the length of the full-length polypeptide.

Preferred specific fragments include fragments comprising one or more residues of any of the fragments of SEQ ID NO:52-119, e.g. two or more, such as three or more, e.g. four or more, such as 5 or more resides, e.g. 6 or more consecutive residues of any of the fragments of SEQ ID NO:52-119. Even more preferred specific fragments include fragments consisting of or essentially consisting of any of the sequences set forth in SEQ ID NO:52-119.

Preferably, fragments of the invention are surface-exposed in an intact Campylobacter jejuni cell or other cell when expressed recombinantly therein. Surface-exposure can be e.g. be determined using a monoclonal antibody specific for said fragment, e.g. as described in Singh et al. (2003) Infect. Immun. 71:3973-3946. Also preferred are fragments which are capable of inducing antibodies that can specifically bind an intact Campylobacter jejuni cell. This can be determined by generating monoclonal antibodies using said fragment and subsequent characterisation of the binding of individual antibodies to intact cells, e.g. as described in Singh et al. (2003) Infect. Immun. 71:3973-3946.

The full-length polypeptides of SEQ ID NO:1-51 as well as the fragments of the invention can be produced recombinantly by conventional techniques known in the art. Suitable host cells can be mammalian cells, e.g. CHO, COS or HEK293 cells. Alternatively, insect cells, bacterial cells or fungal cells can be used. Methods for heterologous expression of polynucleotide sequences in the cell types listed above and subsequent purification of the produced polypeptides, e.g. using a tag sequence

which may be removed after purification, are well-known to those skilled in the art. Alternatively, fragments of the invention can be produced synthetically.

Variants of the invention

In a further main aspect, the invention relates to variants of any of the polypeptides set forth in SEQ ID NO:1-51, such as SEQ ID NO:1-36 or SEQ ID NO:37-51 or variants of fragments of any of the polypeptides set forth in SEQ ID NO:1-51.

When used herein, phrases such as 'a polypeptide having at least 95% sequence identity to SEQ ID NO:X' are used interchangeably with, and are intended to be directed to the same subject-matter as, phrases such as 'the polypeptide of SEQ ID NO:X and variants thereof, wherein the variant has at least 95% sequence identity to said sequence.'

Variants preferably have at least 75% sequence identity, for example at least 80% sequence identity, such as at least 85% sequence identity, for example at least 90% sequence identity, such as at least 91% sequence identity, such as at least 92% sequence identity, for example at least 93% sequence identity, such as at least 94% sequence identity, for example at least 95% sequence identity, such as at least 96% sequence identity, for example at least 97% sequence identity, such as at least 98% sequence identity, for example 99% sequence identity with the given polypeptide or fragment. Sequence identity is determined with any of the algorithms GAP, BESTFIT, or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights.

Preferred variants of a given polypeptide or fragment are variants in which all amino-acid substitutions between the variant and the given reference polypeptide or fragment are conservative substitutions. Conservative amino-acid substitutions refer to the interchangeability of residues having similar side chains. For example, a group of amino acids having aliphatic side chains is glycine, alanine, valine, leucine, and isoleucine; a group of amino acids having aliphatic-hydroxyl side chains is serine and threonine, a group of amino acids having amide-containing side chains is asparagine and glutamine; a group of amino acids having aromatic side chains is phenylalanine, tyrosine, and tryptophan; a group of amino acids having basic side chains is lysine, arginine, and histidine; and a group of amino acids having sulfur-containing side chains is cysteine and methionine. Preferred conservative amino-

acids substitution groups are: valine-leucine-isoleucine, phenylalanine-tyrosine, lysine-arginine, alanine-valine, and asparagine-glutamine.

Variants of a polypeptide or of a fragment thereof also include forms of the polypeptide or fragment wherein one or more amino acids have been deleted or inserted. Preferably, less than 5, such as less than 4, e.g. less than 3, such as less than 2, e.g. only one amino acid has been inserted or deleted. 'Variants' of a polypeptide or of a fragment thereof also include forms of these polypeptides or fragments modified by post-translational modifications of the amino-acid sequence.

Polynucleotides and expression vectors of the invention

In a further aspect, the invention relates to polynucleotides, preferably isolated and/or recombinant polynucleotides, comprising a sequence encoding an antigenic fragment or variant of any of the sequences of SEQ ID NO:1-51; such as a sequence encoding an antigenic fragment or variant of any of the sequences of SEQ ID NO:1-36 or a sequence encoding a antigenic fragment or variant of any of the sequences of SEQ ID NO: 37-51.

Furthermore, the invention relates to expression vectors comprising a sequence encoding a polypeptide which comprises any of the sequences of SEQ ID NO:1-51, or comprises a fragment or variant of any of said sequences. Preferred expression vectors as ones suitable for DNA vaccination. Other preferred expression vectors are ones in which a polynucleotide of the invention is under the control of a promoter that directs expression of the sequence in Escherichia coli or Salmonella. The latter expression vectors are useful in the production of a recombinant virus or recombinant cell of the invention as described herein.

The polynucleotides and expression vectors of the invention can be prepared by standard recombinant DNA techniques well-known to the person skilled in the art.

Recombinant cells of the invention

In a further main aspect, the invention relates to a recombinant cell transformed or transfected with a polynucleotide comprising a sequence encoding a polypeptide, said polypeptide comprising any of the sequences of SEQ ID NO:1-36, or comprising an antigenic fragment or variant of any of said sequences. Preferably, said recombinant cell is an Escherichia coli or Salmonella cell, more preferably an attenuated or reduced-virulence Escherichia or Salmonella cell.

In a further aspect, the invention relates to a recombinant attenuated or reduced-virulence microbial cell, preferably an Escherichia coli or a Salmonella cell transformed or transfected with a polynucleotide comprising a sequence encoding a polypeptide, said polypeptide comprising any of the sequences of SEQ ID NO:37-51, or comprising an antigenic fragment or variant of any of said sequences.

Suitable bacterial strains for use therein have been described in e.g. Makino et al. (2001) Microb. Pathog. 31:1-8; Gentschev et al. (2002) Int. J. Med. Microbiol. 291:577-582; Turner et al. (2001) Infect. Immun. 69:4969-4979; WO99/49026; and WO03/022307 and references therein. Examples of suitable Salmonella strains are CvD908-T7pol (Santiago-Machuca et al. (2002) Plasmid 47:108-119), ATCC 39183, ATCC 53647 and ATCC 53648. Examples of suitable E. coli strains are YT106 and E1392/75-2A.

Methods and uses of the invention

The products defined above can be used to treat or prevent Campylobacter jejuni infections, and/or disease resulting from such infections, in animals or human beings. Preferably, the animal is a chicken, duck, turkey, cow or pig. Preferred human populations are at-risk populations, such as the population of children up to 4 years old, the population of persons in industrialised nations or the population of naive or semi-immune travellers to the developing world.

Treatment and prevention herein include all types of therapeutic treatment and preventive treatment and other treatments to combat Campylobacter jejuni, including but not limited to vaccination, prophylaxis, active immunisation, passive immunisation, administration of antibodies, curative treatment, ameliorating treatment. In particular, passive immunisation using antibodies of the invention is a suitable treatment for immunocompromised individuals.

Thus, in a further aspect, the invention relates to a method for treatment or prevention of Campylobacter jejuni infection in an animal or human being comprising the step of administering any one of the following

- a polypeptide which comprises any of the sequences of SEQ ID NO:1-51, such as any of the sequences of SEQ ID NO:1-36 or any of SEQ ID NO:37-51, or comprises a fragment or variant of any of said sequences,
- a polynucleotide comprising a sequence encoding said polypeptide,
- an expression vector comprising a sequence encoding said polypeptide,

- a recombinant virus or recombinant cell comprising said polynucleotide or said expression vector,
- an antibody capable of specifically binding said polypeptide,
  or
- a composition as defined herein.

Preferably, said administration is done parenterally, intravenously, intramuscularly, subcutaneously, orally or intranasally.

Accordingly, the invention relates to

- a polypeptide which comprises any of the sequences of SEQ ID NO:1-51, such as any of the sequences of SEQ ID NO:1-36 or any of SEQ ID NO:37-51, or comprises a fragment or variant of any of said sequences,
- a polynucleotide comprising a sequence encoding said polypeptide,
- an expression vector comprising a sequence encoding said polypeptide,
- a recombinant virus or recombinant cell comprising said polynucleotide or said expression vector,
- an antibody capable of specifically binding said polypeptide,
  or
- a composition as defined herein.

for use as a medicament.

Preferably, said medicament is a medicament suitable for parenteral, intravenous, intramuscular, subcutaneous, oral or intranasal administration.

In a further aspect, the invention relates to a method for the immunisation of an animal or human being against Campylobacter jejuni infections comprising the step of administrating

- a polypeptide which comprises any of the sequences of SEQ ID NO:1-51, such as any of the sequences of SEQ ID NO:1-36 or any of SEQ ID NO:37-51, or comprises a fragment or variant of any of said sequences,
- a polynucleotide comprising a sequence encoding said polypeptide,
- an expression vector comprising a sequence encoding said polypeptide,
- a recombinant virus or recombinant cell comprising said polynucleotide or said expression vector,

or

- a composition as defined herein.

Preferably, said administration is done parenterally, intravenously, intramuscularly, subcutaneously, orally or intranasally.

Accordingly, in one embodiment the invention relates to use of

- a polypeptide which comprises any of the sequences of SEQ ID NO:1-51, such as any of the sequences of SEQ ID NO:1-36 or any of SEQ ID NO:37-51, or comprises a fragment or variant of any of said sequences,
- a polynucleotide comprising a sequence encoding said polypeptide,
- an expression vector comprising a sequence encoding said polypeptide,
- a recombinant virus or recombinant cell comprising said polynucleotide or said expression vector,

  or
- a composition as defined herein,

for the preparation of a medicament for the immunisation of an animal or human being against Campylobacter jejuni infections.

Preferably, said immunisation induces a protective immune response. Preferably, said medicament is a medicament suitable for parenteral, intravenous;. intramuscular, subcutaneous, oral or intranasal administration.

In a further aspect, the invention relates to the use of an antibody of the invention as defined herein for the manufacture of a medicament for the treatment or prevention of Campylobacter jejuni infections in an animal or human being. Thus, the invention also relates to a method for the treatment or prevention of Campylobacter jejuni infections comprising the step of administering an antibody of the invention as defined herein.

Diagnostic methods of the invention

The combination of being surface-exposed and being present in relatively high copy numbers in cells also makes the 51 polypeptides identified by the inventors highly suitable as targets for detection of Campylobacter jejuni, allowing detection of this organism with high sensitivity.

Accordingly, in a further main aspect, the invention relates to a method for detecting Campylobacter jejuni comprising the steps of

a. providing a biological sample,
b. contacting said sample with an indicator moiety capable of specifically binding any of the polypeptides of SEQ ID NO:1-36, and
c. determining whether a signal has been generated by the indicator moiety.

Preferably, said indicator moiety is capable of specifically binding intact Campylobacter jejuni cells.

In another aspect, the invention relates to a method for detecting a Campylobacter jejuni comprising the steps of

a. providing a biological sample,
b. contacting said sample with an indicator moiety capable of specifically binding any of the polypeptides of SEQ ID NO:37-51, wherein the indicator moiety furthermore is capable of specifically binding intact Campylobacter jejuni cells, and
c. determining whether a signal has been generated by the indicator moiety.

In preferred embodiments, a washing step is performed between the contacting step and the determination step, in order to improve the specificity of detection.

The biological sample can be faeces, urine, a tissue, tissue extract, fluid sample or body fluid sample, such as blood, plasma or serum. Another example of a biological sample is a food sample, such as a meat sample.

The above methods can e.g. be used to diagnose Campylobacter jejuni infections or campylobacteriosis in an individual. In preferred embodiments of the above methods, said indicator moiety does not pass through the outer-membrane of a Campylobacter jejuni cell. A preferred type of said indicator moiety is or comprises an antibody, such as an antibody as defined elsewhere herein.

Those skilled in the art will understand that there are numerous well known clinical diagnostic chemistry procedures in which an indicator moiety can be used to form an binding reaction product whose amount relates to the amount of the ligand,

herein C. jejuni or parts thereof, in a sample. Thus, while exemplary assay methods are described herein, the invention is not so limited.

The present invention also relates to a diagnostic system, preferably in kit form, for assaying for the presence, and preferably also the amount, of Campylobacter jejuni in a biological sample. Methods for the preparation of diagnostic kits have e.g. been described in US 5,470,958 and references therein.

The diagnostic system includes, in an amount sufficient to perform at least one assay, an indicator moiety according to the present invention, preferably as a separately packaged reagent, and more preferably also instructions for use. Packaged refers to the use of a solid matrix or material such as glass, plastic (e.g., polyethylene, polypropylene or polycarbonate), paper, foil and the like capable of holding within fixed limits an indicator moiety of the present invention. Thus, for example, a package can be a glass vial used to contain milligram quantities of a contemplated labelled indicator moiety preparation, or it can be a microtiter plate well to which microgram quantities of a contemplated indicator moiety has been operatively affixed, i.e., linked so as to be capable of binding a ligand.

"Instructions for use" typically include a tangible expression describing the reagent concentration or at least one assay method parameter such as the relative amounts of reagent and sample to be admixed, maintenance time periods for reagent/sample admixtures, temperature, buffer conditions and the like.

In most embodiments, the diagnostic method and system of the present invention include as a part of the indicator moiety, a label or indicating means capable of signalling the formation of a binding reaction complex containing an indicator moiety complexed with the preselected ligand (i.e. a polypeptide comprising any of the sequences of SEQ ID NO:1-51 and/or a fragment thereof). Such labels are themselves well-known in clinical diagnostic chemistry.

The labelling means can be a fluorescent labelling agent that chemically binds to antibodies or antigens without denaturing them to form a fluorochrome (dye) that is a useful immunofluorescent tracer. Suitable fluorescent labelling agents are fluorochromes such as fluorescein isocyanate (FIC), fluorescein isothiocyante (FITC), 5-dimethylamine-1-naphthalenesulfonyl chloride (DANSC), tetramethylrhodamine isothiocyanate (TRITC), lissamine, rhodamine 8200 sulphonyl chloride (RB 200 SC). Other examples of suitable fluorescent materials include umbelliferone,

dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin and the like. A description of immunofluorescence analysis techniques is found in DeLuca, "Immunofluorescence Analysis", in Antibody As a Tool, Marchalonis, et al., eds., John Wiley & Sons, Ltd., pp. 189-231 (1982).

Radioactive elements can be useful as labelling agents. An exemplary radiolabeling agent is a radioactive element that produces gamma ray emissions. Elements which themselves emit gamma rays, such as ^{124}I, ^{125}I, ^{128}I, ^{132}I and ^{51}Cr represent one class of gamma ray emission-producing radioactive element indicating groups. Particularly preferred is ^{125}I. Another group of useful labelling means are those elements such as ^{11}C, ^{18}F, ^{15}O and ^{13}N which themselves emit positrons, or beta emitters, such as ^{111}indium of ^{3}H. Other suitable radioactive materials include ^{131}I and ^{35}S.

Detection using antibodies can, in other embodiments, be facilitated by coupling the antibody to another detectable substance, such as an enzyme, a prosthetic group, a luminescent materials, or a bioluminescent material. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include Streptavidin/biotin and avidin/biotin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin.

In preferred embodiments, the indicating group is an enzyme, such as horseradish peroxidase (HRP) or glucose oxidase. In such cases where the principal indicating group is an enzyme such as HRP or glucose oxidase, additional reagents are required to visualise the fact that a indicator-moiety/ligand complex (immunoreactant) has formed. Such additional reagents for HRP include hydrogen peroxide and an oxidation dye precursor such as diaminobenzidine. An additional reagent useful with glucose oxidase is 2,2'-amino-di-(3-ethyl-benzthiazoline-G-sulfonic acid).

The linking of labels, i.e. labelling of polypeptides such as antibodies, is well known in the art. For instance, proteins can be labelled by metabolic incorporation of radioisotope-containing amino acids provided as a component in the culture medium. See, for example, Galfre et al., Meth. Enzymol., 73:3-46 (1981). The techniques of protein conjugation or coupling through activated functional groups are particularly applicable. See, for example, Aurameas, et al., Scand. J. Immunol., Vol.

8 Suppl. 7:7-23 (1978), Rodwell et al. (1984) Biotech. 3:889-894, and U.S. Pat. No. 4,493,795.

Various diagnostic assays employing the above indicator moieties can be set up to test samples for *Campylobacter jejuni*. Exemplary assays are described in detail in Antibodies: A Laboratory Manual, Harlow and Lane (eds.), Cold Spring Harbor Laboratory Press, 1988. Representative examples of such assays include: countercurrent immuno-electrophoresis (CIEP), radioimmunoassays, radioimmuno-precipitations, enzyme-linked immuno-sorbent assays (ELISA), dot blot assays, inhibition or competition assays, and sandwich assays, immunostick (dipstick) assays, simultaneous immunoassays, immunochromatographic assays, immunofiltration assays, latex bead agglutination assays, immunofluorescent assays, biosensor assays, and low-light detection assays (see e.g. also U.S. 4,376,110 and 4,486,530).

In one embodiment, the diagnostic kits of the present invention can be used in an "ELISA" format to detect the quantity of a preselected ligand in a fluid sample.. "ELISA" refers to an enzyme-linked immunosorbent assay that employs an antibody or antigen bound to a solid phase and an enzyme-antigen or enzyme-antibody conjugate to detect and quantify the amount of an antigen present in a sample and is readily applicable to the present methods. Thus, in some embodiments, an indicator moiety of the present invention can be affixed to a solid matrix to form a solid support that comprises a package in the subject diagnostic systems. A reagent is typically affixed to a solid matrix by adsorption from an aqueous medium although other modes of affixation applicable to polypeptides, such as antibodies, can be used that are well known to those skilled in the art. Useful solid matrices are also well known in the art. Such materials are water insoluble and include the cross-linked dextran available under the trademark SEPHADEX from Pharmacia Fine Chemicals (Piscataway, N.J.); agarose; beads of polystyrene beads about 1 micron to about 5 millimetres in diameter available from Abbott Laboratories of North Chicago, Ill.; polyvinyl chloride, polystyrene, cross-linked polyacrylamide, nitrocellulose- or nylon-based webs such as sheets, strips or paddles; or tubes, plates or the wells of a microtiter plate such as those made from polystyrene or polyvinylchloride.

A further diagnostic method may utilise the multivalency of an antibody composition of one embodiment of this invention to cross-link ligands, thereby forming an aggregation of multiple ligands and polypeptides, producing a precipitable aggregate. This embodiment is comparable to the well known methods of immune precipitation. This embodiment comprises the steps of admixing a sample with

a composition comprising an antibody of this invention to form a binding admixture under binding conditions, followed by a separation step to isolate the formed binding complexes. Typically, isolation is accomplished by centrifugation or filtration to remove the aggregate from the admixture. The presence of binding complexes indicates the presence of the preselected ligand to be detected.

Binding partners and inhibitors of polypeptides of the invention

The surface-localisation of the 51 polypeptides to which this work relates makes them highly suitable as targets for binding partners, such as inhibitors. Surface-located polypeptides of a pathogenic microorganism often interact with the host organism. Thus, any type of binding partner of a surface-located polypeptide may interfere with host-pathogen interaction. Binding partners thus often antagonise the pathogenicity (virulence) of a microorganism. A binding partner may also be an inhibitor of the polypeptide it binds.

Thus, in a further main aspect, the invention relates to methods for the identification of binding partners of the surface-located polypeptides set forth in SEQ ID NO:1-51. Such methods may be biochemical or cell-based.

Biochemical methods

In a main aspect, the invention relates to a method for identifying a binding partner of any of the polypeptides of SEQ ID NO:1-36 or a fragment thereof, comprising the steps of

a. providing any of the polypeptides of SEQ ID NO:1-36 or a fragment thereof,
b. contacting said polypeptide or fragment with a putative binding partner, and
c. determining whether said putative binding partner is capable of binding to said polypeptide or fragment.

In preferred embodiments of this method, the polypeptide or fragment thereof is provided immobilised on a solid support, such as e.g. a column or microtiter plate, and, after the contacting step, it is determined whether or not the putative binding partner has bound to the solid support. Immobilisation of the polypeptide or fragment thereof may be through direct binding to the solid support, or through indirect binding e.g. using a specific antibody. In preferred embodiments, a washing step is performed between the contacting step and the determination step, in order to

improve the specificity of detection. In further preferred embodiments, the putative binding partner is complexed with a detectable label. The putative partner may be labelled before the contacting takes place. Alternatively, labelling may also be performed after the contacting step. Furthermore, in some embodiments of this method, immobilisation may be performed after the polypeptide or fragment thereof has been bound to the binding partner. In preferred embodiments, the method is a screening method wherein the method is repeated for a plurality of putative binding partners. Suitable methods to determine binding are well-known in the art, and several of them have been referred to elsewhere herein.

In another aspect, a host-derived binding partner of a polypeptide selected from the group of SEQ ID NO:1-51, such as any of SEQ ID NO:1-36 or any of SEQ ID NO:37-51 may be identified as follows: purified host membranes are electrophoretically separated, blotted over to a membrane and incubated with the polypeptide of interest or fragment thereof. Binding can then be detected using antibodies specific for the polypeptide of interest or fragment thereof. The host binding partner to which the polypeptide or fragment thereof has bound can subsequently be identified by elution from the blot and subsequent analysis by mass spectrometry, or by any other technique known in the art.

If the binding partner of a surface-located polypeptide of a pathogenic organism is a host-derived molecule, then such an interaction between the surface-located polypeptide and the host may be important for the virulence of the bacterium. Compounds that interfere with the interaction of the surface-located polypeptide and the host-derived binding partner may thus be suitable for prevention or treatment of *Campylobacter jejuni* infections. Accordingly, another method of the invention relates to a method of identifying an inhibitor of the interaction of any of the surface-located Campylobacter jejuni polypeptides of SEQ ID NO:1-51, such as any of SEQ ID NO:1-36 or any of SEQ ID NO:37-51, with a host-derived binding partner comprising the steps of:

a. providing any of the polypeptides of SEQ ID NO:1-51, such as any of SEQ ID NO:1-36 or any of SEQ ID NO:37-51, or a fragment thereof,
b. providing a host-derived binding partner of said polypeptide (identified as described above or by any other method),
c. contacting said polypeptide with said host-derived binding partner in the absence of a putative inhibitor of said interaction,

d. contacting said polypeptide with said host-derived binding partner in the presence of said putative inhibitor,
and
e. determining whether the strength of the binding of said polypeptide to said host-derived binding partner resulting from step d. is reduced as compared to that resulting from step c.

In some embodiments, step c. and d. may be performed in two different sample compartments. In other embodiments, step d. may be performed by adding the putative inhibitor to the mixture of step c. In preferred embodiments, the method is repeated for a plurality of putative inhibitors.

Of particular interest are binding partners that inhibit an activity of a surface-located polypeptide. Such activity may be enzymatic activity, transport activity, or any type of other biochemical or cellular activity, preferably enzymatic activity.

Preferred host-derived binding partners are host polypeptides and host lipids. Binding may e.g. be determined as described by Szymanski and Armstrong (1996) Infect. Immun. 64:3467-3474.

In preferred embodiments of the above described biochemical methods, the binding between the binding partner and the surface-located polypeptide or fragment thereof has a dissociation constant or Kd less than 5×10^{-6}M, such as less than 10^{-6}M, e.g. less than 5×10^{-7}M, such as less than 10^{-7}M, e.g. less than 5×10^{-8}M, such as less than 10^{-8}M, e.g. less than 5×10^{-9}M, such as less than 10^{-9}M, e.g. less than 5×10^{-10}M, such as less than 10^{-10}M, e.g. less than 5×10^{-11}M, such as less than 10^{-11}M, e.g. less than 5×10^{-12}M, such as less than 10^{-12}M. Dissociation constants can e.g. be determined by surface plasmon resonance analysis.

Cell-based methods

Reducing the level of a surface-located polypeptide, by deletion or disruption of the structural gene for it or by down-regulating gene expression (see below), may affect a bacterial cell. The cell may become more sensitive to cytotoxic compounds. Especially for surface-located polypeptides, a reduction of their level may affect the function of the cell's exterior parts, such as the outer membrane or cell wall, in preventing compounds of entering the cell. Thus, reduction of the level of an

surface-located polypeptide can make a cell more 'permeable' for various compounds.

Thus, an aspect of the present invention relates to a method for identifying a compound with antibacterial activity against Campylobacter jejuni comprising the steps of

a. providing a sensitised cell which has a reduced level of any of the polypeptides of SEQ ID NO:1-36, and
b. determining the sensitivity of said cell to a putative antibacterial compound, for instance by a growth assay.

Preferably, the method is a screening method wherein the procedure is repeated for a plurality of putative antibacterial compounds. Preferred putative antibacterial compounds are ones that do not pass through the outer membrane of a Campylobacter jejuni cell.

Furthermore, the invention relates to a method for identifying a compound with antibacterial activity against Campylobacter jejuni comprising the steps of

a- providing a sensitised cell which has a reduced level of any of the polypeptides of SEQ ID NO:37-51, and
b. determining the sensitivity of said cell to a putative antibacterial compound, for instance by a growth assay, wherein the putative antibacterial compound is not capable of passing through the outer membrane of a Campylobacter jejuni cell.

Preferably, the method is screening method wherein the procedure is repeated for a plurality of putative antibacterial compounds.

The rationale behind this approach is that a cell with a lower level of the surface-located polypeptide will exhibit increased sensitivity to cytotoxic compounds, allowing identification of antibacterial compounds with low potency that are missed when using wild-type cells for the assay. Compounds identified by this method will be often need to be modified in order to improve potency. This can be done by chemical modification.

Inhibition of the activity of a surface-located polypeptide may affect the viability (i.e. survival, growth and/or proliferation) of the bacterium. Of particular interest is inhibition of surface-located polypeptides that are essential for viability of Campylobacter jejuni. Essentiality of a Campylobacter jejuni gene may e.g. be

investigated as described in WO 02/077183. Inhibitors of essential surface-located polypeptides may not need to enter the bacterial cell to be able to affect its viability. Thus, generally fewer requirements are posed on the structure of an inhibitor of an essential surface-located target polypeptide than on an inhibitor of an intracellular target, to be effective as an antibacterial agent.

Accordingly, the invention relates to a method for finding an inhibitor of any of the polypeptides of SEQ ID NO:1-36 comprising the steps of

a. providing two cells which differ in the level of any of the polypeptides of SEQ ID NO:1-36,
b. determining the sensitivity of said cells to a putative inhibitor, for instance by a growth assay, and
c. determining whether said two cells are differently affected by the presence of said putative inhibitor.

Preferably, the method is repeated for a plurality of putative inhibitors. Preferred inhibitors are ones that do not pass through the outer membrane of a Campylobacter jejuni cell.

Furthermore, the invention relates to a method for finding an inhibitor of any of the polypeptides of SEQ ID NO:37-51 comprising the steps of

a. providing two cells which differ in the level of any of the polypeptides of SEQ ID NO:37-51,
b. determining the sensitivity of said cells to a putative inhibitor, for instance by a growth assay, wherein the putative inhibitor is not capable of passing through the outermembrane of a Campylobacter jejuni cell, and
c. determining whether said two cells are differently affected by the presence of said putative inhibitor.

Preferably, the method is repeated for a plurality of putative inhibitors.

The rationale behind this approach is that the viability of a cell with a lower activity of the essential polypeptide will be more affected by an inhibitor of the polypeptide than the viability of the cell with a higher level. If the two cells are differently affected, this is an indication that the inhibitor acts on the target or at least in the same biochemical pathway.

In some embodiments of the method, the two cells with different activity of the polypeptide of interest are a wild-type cell (or other cell with wild-type activity of the gene of interest) and a sensitised cell with a reduced activity of the polypeptide of interest. In some embodiments, the different or reduced level in the sensitised cell can be a different or reduced expression level of the gene of interest (resulting in a different or reduced copy number of the polypeptide). This can be accomplished by putting the gene under control of a regulatable promoter or by regulatable expression of an antisense RNA which inhibits translation of an mRNA encoding the essential polypeptide. In other embodiments, the different or reduced activity can be a different or reduced activity of the polypeptide of interest, e.g. due to a mutation, such as a temperature-sensitive mutation.

Suitable ways of generating sensitised cells and of using these in screening for inhibitors have been described in WO 02/077183. Sensitised cells may be obtained by growing a conditional-expression *C. jejuni* mutant strain in the presence of a concentration of inducer or repressor or other conditions which provide a level of a gene product required for bacterial viability such that the presence or absence of its function becomes a rate-determining step for viability. Regulatable promoters for Campylobacter jejuni have e.g. been described in Kelana et al. (2003) J Food Prot 66:1190-1197 and Dedieu et al. (2002) Appl Environ. Microbiol. 68:4209-4215. The sub-lethal expression of the target gene may be such that growth inhibition is at least about 10%, such as at least about 25%, e.g. at least about 50%, such as at least about 75%, e.g. at least 90%, such as at least 95%.

In another embodiment of the cell-based assays of the present invention, sensitised cells are obtained by reduction of the level activity of a polypeptide required for bacterial viability using a mutation, such as a temperature-sensitive mutation, in the polypeptide. Growing such cells at an intermediate temperature between the permissive and restrictive temperatures produces cells with reduced activity of the gene product. It will be appreciated that the above method may be performed with any mutation which reduces but does not eliminate the activity or level of the gene product which is required for bacterial viability. This approach may also be combined with the conditional-expression approach. In this combined approach, cells are created in which there is a temperature-sensitive mutation in the gene of interest and in which this gene is also conditionally-expressed.

When screening for inhibitors of an essential polypeptide, growth inhibition can be measured by directly comparing the amount of growth, measured by the optical density of the culture relative to uninoculated growth medium, in an experimental sample with that of a control sample. Alternative methods for assaying cell proliferation include measuring green fluorescent protein (GFP) reporter construct emissions, various enzymatic activity assays, and other methods well known in the art. Other parameters used to measure viability include e.g. colony forming units. The above method may be performed in solid phase, liquid phase, a combination of the two preceding media, or *in vivo*. Multiple compounds may be transferred to agar plates and simultaneously tested using automated and semi-automated equipment.

Cell-based assays of the present invention are capable of detecting compounds. exhibiting low or moderate potency against the target molecule of interest because such compounds are substantially more potent on sensitised cells than on non-sensitised cells. The effect may be such that a test compound may be two to several times more potent, e.g. at least 10 times more potent, such as at least 20 times more potent, e.g. at least 50 times more potent, such as at least 100 times more potent, e.g. at least 1000 times more potent, or even more than 1000 times more potent when tested on the sensitised cells as compared to non-sensitised cells.

A mutant Campylobacter jejuni strain that overexpresses a surface-located polypeptide can also be used to identify a compound that inhibits such a polypeptide. If the compound is cytotoxic, overexpression of the target polypeptide can make cells more resistant. Thus, the invention also relates to a method for finding an inhibitor of any of the surface-located Campylobacter jejuni polypeptides of SEQ ID NO:1-51, such as any of SEQ ID NO:1-36 or any of SEQ ID NO:37-51 comprising the steps of

a. providing two cells which differ in the activity of any of the surface-located Campylobacter jejuni polypeptides of SEQ ID NO:1-51, such as any of SEQ ID NO:1-36 or any of SEQ ID NO:37-51, wherein one cell contains a substantially wild-type copy number of said polypeptide and the other cell contains higher than wild-type copy number of said polypeptide,
b. determining the sensitivity of said cells to a putative inhibitor, for instance by a growth assay, and

c. determining whether or not said two cells are differently affected by the presence of said putative inhibitor.

Overexpression may be achieved using strong promoters or by introducing multiple copies of the structural gene for a surface-located polypeptide. Strong Campylobacter jejuni promoters have been described by Wosten et al. (1998) J. Bacteriol. 180:594-599. As also overexpression of polypeptides that are not the cellular target of an inhibitor can make cells resistance to an inhibitor, inhibition of the target polypeptide of interest by a putative inhibitor will need to be verified by other means, such as e.g. a biochemical assay.

In addition to inhibitors of a biochemical or other cellular activity of a surface-located polypeptide, the cellular methods described above can be used to identify compounds that reduce the expression level of a target, and thereby its copy number, e.g. by interfering with gene regulation.

In preferred embodiments of the any of the cell-based- or biochemical methods for finding binding partners or inhibitors, the method is repeated for a plurality of candidate compounds.

In a further aspect, the invention relates to the mutant Campylobacter jejuni strains used in the cell-based methods described herein, such as strains in which the gene encoding the surface-located polypeptide is placed under the control of a heterologous regulatable promoter, strains carrying temperature-sensitive alleles of the surface-located polypeptides, and strains overexpressing the surface-located polypeptides.

Other methods of interfering with bacterial growth by targeting surface-located polypeptides, such as any of the polypeptides of SEQ ID NO:1-36 include suppression of gene expression using specific antisense molecules, such antisense RNA or DNA, and using ribozyme molecules specific for mRNA encoding the essential surface-located polypeptides.

Exampl s

Strategy:

The experimental steps in the project as follows: Isolate surface proteins by low pH elution. Analyse by 2-D gels and mass spectrometry. Clone into E. coli expression vector. Produce recombinant protein, immunise mice, challenge the immunised mice with Campylobacter jejuni and look for protection against disease and intestinal colonisation. E. coli and Salmonella surface localisation is also assessed (if positive, there is potential for use in attenuated vector strains).

Bacterial culture:

Campylobacter jejuni (C.j.) strain 0:19 (CCUG 10950), a clinical isolate from human faeces was obtained from the Culture Collection, University of Goteborg (CCUG) in Sweden. It was routinely grown on blood agar plates at 37°C in atmosphere of 10% CO_2, 5% O_2.

Surface proteins extraction:

Bacteria were grown overnight on blood agar plates, harvested into 50 mM Tris pH7.8 and pelleted by centrifugation at 6000g for 5 minutes. The pellet was resuspended in 0.2 M glycine pH2.2 and the bacterial suspension was gently mixed at room temperature for 10 minutes. Bacteria were pelleted again by centrifugation at 6000g for 5 minutes, supernatant containing surface proteins was collected, neutralised with NaOH and frozen at –80°C. The sample was desalted on Amersham HiTrap desalting column before 2-D gel electrophoresis.

2-D gel electrophoresis:

Two-dimensional gel electrophoresis was performed either on the Ettan Dalt 2 system (Amersham Biosciences) or on the Novex NuPage system (Invitrogen) according to the manual provided with the gel system.

In brief: First dimension runs were performed on either 7 cm or 24 cm pre-cast IPG strips (pH range 3-10 or 6-11) using the Ettan IPGphor isoelectric focusing system (Amersham Biosciences) according to the manufacturer's instructions. Isofocusing was performed at the following conditions: 7 cm pH 3-10 strips:8000 Vh, 7 cm pH 6-11 strips:16000Vh, 24 cm pH 3-10 strips: 52000Vh. The second dimension was performed using pre-cast 12.5 % gels (Amersham Biosciences) at 5W per gel for 15

min then total 170 W for 4-6 hours for 24 cm strips. The 7 cm strips were run on the Novex NuPage system (Invitrogen) using pre-cast 4-12% gels (Invitrogen) at 200 volts for 40 minutes. Gels were silver stained according to a modified method described originally by Mortz et al. (2001) Proteomics 1(11), 1359-1363, and spots for mass spec analysis were picked using the Ettan Spot Picker from Amersham according to the manufacturer instructions.

Mass Spectrometry:

Specific protein spots were spot-picked, and placed in Milli-Q water. These gel plugs were washed in 50mM NH_4HCO_3 / 50% ethanol and dehydrated by incubation in 96% ethanol. Reduction and alkylation was performed by incubating in reducing solution (10 mM DTT, 50 mM NH_4HCO_3) at 56°C followed by a room temperature incubation in alkylation solution (55 mM iodoacetamide, 50 mM NH_4HCO_3) in the dark. Two cycles of washing and dehydration were then performed prior to the addition of 5 ul trypsin solution (12.5 ng/ul Promega trypsin in 50 mM NH_4HCO_3, 10% Acetonitrile). Then an additional amount of sodium bicarbonate solution was added and the digests were incubated overnight at 37°C. Trifluoroacetic acid was added to the overnight digest followed by incubation with shaking.

Parts of the extract were used in MALDI-TOF peptide mass fingerprint analysis (Reflex IV, Bruker Daltonics, Germany) and the peaklist was used in database searching against a specific Campylobacter jejuni database. The Mascot search program and scoring algorithm (Matrix Science, UK) was used in database searching. Peptide mass tolerance was set to 60 ppm and 0.5 Da, respectively. Search parameters were adjusted to include oxidation of Met, the addition of Carbamidomethyl groups to Cys, and trypsin was allowed to miss one cleavage site per peptide.

The fragments given in list 1 (see below) were identified. In total 51 different Campylobacter jejuni proteins were identified using this procedure. The full-length sequences of these proteins are given in SEQ ID NO:1-51. The proteins in the sequence listing are functionally classified according to the classification from the Sanger Institute. All proteins which were predicted from genomic sequence but had not been characterised before, and did not have any homology to previously characterised proteins, were classified as hypothetical by the Sanger institute. Those which had homology to known proteins were named as the corresponding known protein with the pre-fix "probable" or "putative", depending on the degree of

homology. Some proteins have small motifs, which did not allow to assign a precise biochemical/metabolic function to them, but did allow to state the fact that they possess of a certain feature, such as nucleotide binding motifs, membrane attachment sites, etc. Putative periplasmic proteins were classified as such on a similar basis – they possess a short (4-6 amino acids) N-terminal motif, which may mediate transport to the periplasm.

Bioinformatic studies:

Antigenicity index studies were performed using the default parameters determined using Lasergene sequence analysis software from the company DNAStar (Burland, TG (2000) Methods Mol. Biol. 132:71-91). The sequences set forth in SEQ ID NO:52-119 are predicted to be particularly antigenic fragments of their corresponding full-length polypeptides.

Cloning and expression in E. coli:

Genes corresponding to the proteins of interest were PCR amplified, operately linked to a His-tag, and the resulting construct was cloned into an E. coli expression vector comprising an IPTG-inducible promoter. Resulting plasmids were transformed into E. coli BL21(DE3) strain and protein expression was induced with 0.5 mM IPTG. Glycine eluate was prepared as above and analysed for the presence of the recombinant Campylobacter jejuni protein by three independent methods: Coomassie staining, Western blotting with anti-his tag antibody, and mass spec analysis. Recombinant protein was purified from cultures induced overnight using NTA-Ni agarose (Qiagen) according to the manufacturer's instructions. For eight transformed E. coli strains (the ones expressing Cj0092, Cj0143c, Cj0420, Cj0715, Cj0772c, Cj1018c, Cj1380 and Cj1643) surface-localisation was determined out as described above. All eight proteins were found on the cell-surface of E. coli.

Mouse immunisation and challenge:

Mice are immunised with recombinant protein subcutaneously 3 times (day 0, 14, 28). The antibody-response is monitored in blood and gastrointestinal secretion 7 days after each immunisation. On day 42, mice are challenged intranasally with 10^9 cfu *C. jejuni* prepared as below. Mice are observed for weight loss and clinical signs of illness for 5-7 days. Several organs are analysed for *C. jejuni* infection.

For colonisation studies, at approximately 4-5 weeks post-vaccination, mice are challenged orally with 10^8 cfu C. jejuni and fecal shedding of Campylobacter jejuni is monitored for 14-21 days. Animals are considered colonisation negative if *C. jejuni* is not detected in three consecutive fecal samples.

C. jejuni for challenge is grown o/n on blood plates at 42°C, harvested into BHI/1%YE and diluted to OD 0.05. 75 cm^2 flasks containing 20 ml of BHI agar are seeded with 25 ml of this starter culture and grown o/n at 42°C. Bacteria are harvested by centrifugation, washed in PBS and finally resuspended in sterile PBS to the desired density.

Results:

Sixteen mice per antigen (SEQ ID NO:1 (Cj0092), SEQ ID NO:8 (Cj0143c), SEQ ID NO:43 (Cj0420) and SEQ ID NO:46 (Cj0772c)) were immunised with 1µg, 5µg, 10µg or 25µg of corresponding recombinant protein (4 animals for each dose). A blood sample of 200 µl blood ml was drawn from the retro orbital plexus at day 7, left for 1 hour to coagulate, centrifuged for 10 min at 3500 G, and serum was collected. Immune response was assessed by performing Western blot analysis using purified recombinant protein and dilutions of above serum samples (see figure 1). The following specific antibody titres were obtained: at least 1:100 for SEQ ID NO:1, at least 1:50 for SEQ ID NO:8, at least 1:4 for SEQ ID NO:43 and at least 1:50 for SEQ ID NO:46. In another experiment, antibody against Cj0092 (SEQ ID NO:1) from two animals was further diluted: 1:50, 1:50, 1:100, 1:200, 1:400, 1:800, 1:1600, 1:3200, and 1:6400. 100ng of purified Cj0092 antigen was loaded on the gel, blotted and probed with the different dilutions of mouse anti-Cj0092 antibody. The antigen could be seen in all dilutions of the antibodies (figure 2).

Salmonella surface localisation studies:

An attenuated Salmonella strain carrying the T7 polymerase gene is transformed with a plasmid suitable for expression of Campylobacter jejuni genes in this organism. Surface localisation is assayed as above.

Immunisation with whole cell vaccine:

E. coli and/or Salmonella strains carrying the protein of interest on the surface are used in immunisation studies, as both killed and live vaccines.

List 1: Fragments of surface-located C. jejuni polypeptides

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Sequence: AnrP544820

AKVEKPLNR
DILKDCGIK
DIPLVNGYPLR
GEMKIIESMPIR
GTQWGYGAVACGR
GYYEIWAR
IHDGEKMEGSYK
IIESMPIR
LNGEETSPISR
LVCGGYPASTSGK
NDAVYIGYYGIDTK
NNGLPPSLETIK
NNGLPPSLETIKER
SYTIEDLK
SYTIEDLKK
TYTYALTVECGGNGR
VEKPLNR
VPVNPVKPGDFNYK

==========

Sequence: AnrP372217

ALFEHGTK
ARVLLMLALTK
IQEYFLK
IQEYFLKY
KIQEYFLK
LGFISAEDLNPQK
LGFISAEDLNPQKAR
LTSLPKVDILYSYSNDGSGVAAK
NAPFDVSK
NAPFDVSKLTSLPK
NQKDVLK
THSLNVDAFSSPDFGDLGYIVDGK
VDILYSYSNDGSGVAAK
VFFYNNVIK
VLLMLALTK
VVVSSRVVAGCVAVSDSDEK

==========

Sequence: AnrP501075

EGVEYFKELSK
KLFEENCVACHGER
LEGDFFAK
LFEENCVACHGER
MNFPNRPADPVR
MPITTTENR
NLSINDVPK
RPVQEWPNK
YGIELLSK

==========

Sequence: AnrP630851

AISEYLPK

AISEYLPKDTK
ALKDLGIDTNSLSEDR
AMLNLQSEFIR
DGKTFYTGK
DLGIDTNSLSEDR
DLGIDTNSLSEDRK
DTKGFLNEYGIR
EFDELPK
EFDELPKGDK
ETALTMADAAIIEFINTNLSLKDER
FYSYENLANTNEALNSK
GDKVDQILNK
GEYDVGVVAVISNK
GFLNEYGIR
IQNYEADNSTNAK
KTNILEDR
KWSYTSENGIEHVGAVR
LTQLAGAQLDK
LTQLAGAQLDKALK
LVYDENGAPIILSYGNWGYVADPSNAK
QLAKDMALAR
QSINVNDSSTQEQTQNITNIIDK
QSINVNDSSTQEQTQNITNIIDKVNSK
SIEDFFEEFADNFGIEYGITK
STVAVNDTDPQFAQALQNAYQK
TLLKQEFLNK
TMTNAIGSMSGLVPVQTIVTQR
TNILEDR
TNILEDRAK
TTGDTYEEIIK
WSYTSENGIEHVGAVR

==========

Sequence: AnrP666574

ADTYEINSVEQDANGK
DANYQTQEGGGVNLGF
DNSLSANETALK
EDAINNAIIEAIGK
ENTGRVESK
FSNTLSMK
FSNTLSMKVNLK
FSYAKITEGSVK
GIGSALQQK
GRADTYEINSVEQDANGK
IAGDILNAIYPLK
IISDLLQSR
KFNVLDR
MSGVSINSLK
MSGVSINSLKK
RGIGSALQQK
SGDAASDEVYKLK
SITVFDSTPDAAK
SITVFDSTPDAAKR
SKTEIEVIVDYR
SNTSVSTDNSGSNIQDNYSEQISK
SSTGEGTGLTR
SSTGEGTGLTREDAINNAIIEAIGK
TEIEVIVDYR
TGSIEITR

TGSIEITRTSPK
TSNLTGKSK
VESKTGSIEITR
VGDICRPLSNTGSGNGYTIGR
VIKDTYTK
VNLKDNSLSANETALK
YQAPGLSADNRR
YTANVTIFK
==========
Sequence: AnrP758295

ADEISSIIK
ADEISSIIKER
AIDALVPIGR
AIDALVPIGRGQR
AINEFKANHL
ALDSDLEEK
ALDSDLEEKLAK
ATKQVSGTLR
DNAKHALIVYDDLSK
EAYPGDVFYLHSR
EAYPGDVFYLHSRLLER
ELIIGDRQTGK
ELQAFAQFASDLDEASR
ELQAFAQFASDLDEASRK
EMSLILR
ERIENFDLNLEIEETGK
FKADEISSIIK
GEGLKEGASVK
GFLDDIAVSR
GFLDDIAVSRIK
GMALNLEESSVGIVILGK
GQGVICIYVAIGQK
GQRMVELLK
GVINANEYR
GVINANEYRFVEEK
HALIVYDDLSK
HALIVYDDLSKHAVAYR
HPDIFEQIR
IENFDLNLEIEETGK
IENFDLNLEIEETGKIISVADGVAK
IISVADGVAK
IISVADGVAKVYGLK
IKEFEDGIYPFIEAK
KALDSDLEEK
KSVHEPLHTGIK
LAKAINEFK
LDLAQYR
LLKVPVGEALIGR
NIMAGEMVEFENGDK
QLERGQR
QPPYSPLSVEK
QPPYSPLSVEKQVVLIFAGTK
QSTVAQVVK
QTGKTTVAVDTIISQR
QVSGTLRLDLAQYR
QVVLIFAGTK
QVVLIFAGTKGFLDDIAVSR
RPPGREAYPGDVFYLHSR

SVHEPLHTGIK
TTVAVDTIISQR
VPVGEALIGR
VPVGEALIGRVVNALGEPIDAK
VVNALGEPIDAK
VVNALGEPIDAKGVINANEYR
VYGLKNIMAGEMVEFENGDK
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Sequence: AnrP732169

AEALGAPISVPVGEK
AIAEKGIYPAVDPLDSTSR
DEMGLDVLMFIDNIFR
DPPAFEDQSTK
DPPAFEDQSTKSEIFETGIK
EGNDLYNEMK
EGNDLYNEMKESNVLDK
ESNVLDKVALCYGQMNEPPGAR
FLSQPFFVAEVFTGSPGK
FSQSGSEMSALLGR
GIYPAVDPLDSTSR
GLKAEALGAPISVPVGEK
GVQSVLQK
HSGYSVFAGVGER
IALTGLTMAEYFR
IFNVTGDLIDEGEEISFDKK
IPSAVGYQPTLASEMGK
LVLEVAAHLGDNR
LVVERAR
MLDPNIIGEEHYK
MLDPNIIGEEHYKVAR
SEIFETGIK
TIAMDMTDGLVR
TREGNDLYNEMK
VALCYGQMNEPPGAR
VGLFGGAGVGK
VRTIAMDMTDGLVR
VVDLLAPYAK
WAIHRDPPAFEDQSTK
YDHLPENAFYMVGNIDEAIAK
YISLEDTIAGFK
==========
Sequence: AnrP511634

DFLVYSSR
DNSNLSDENLKK
DQPDVYLYDLNTK
EPNQAGVFNIYLMSINSDYIR
EQTLFYYTAYDHDKPTLYR
FSSDGGSIVFIK
IIVKDNSNLSDENLK
ILSSGGMVVASDVNVDGSK
KSQIIMADYTLTYQK
LGYPNIFMQDLNSNSAEQVVFHGR
LLVTMAPK
LLVTMAPKDQPDVYLYDLNTK
NGNTLSLNVK
NLTQLTNYSGIDVNGNFIGSDDSK
NNSAVSTYKDFLVYSSR

QLTANGKNLFPR
SEQTYTLNGLEQYPFLAHK
SFYNIIVNDLK
SQIIMADYTLTYQK
TFYFPLR
VGKIQSIDW
VIVDGGLNLFPK
YDLNTNK
YLGAQSALGVIR
==========
Sequence: AnrP57234

DLQKLITLMK
EFVVYHPSWTYFAK
EFVVYHPSWTYFAKR
ENLDKFLAELDSLNLQIASK
FKQNFPK
FLAELDSLNLQIASK
FLAELDSLNLQIASKLEK
IDHLSYDWENELLK
IYKIDHLSYDWENELLK
LEKSDIYFTIGLEFEK
LITLMKDK
LQVINMQK
NLEQEQNTSSNLVSVSIAPQAFFVK
NLEQEQNTSSNLVSVSIAPQAFFVKK
NREFVVYHPSWTYFAK
QNFPKLQVINMQK
RYNLTQIPVEILGK
SDIYFTIGLEFEK
TADAFSHNL
TLAKECDAK
VFTDKFK
VIFVQNGFPENAAK
YNLTQIPVEILGK
YNLTQIPVEILGKEPK
YPQNENLYK
YPQNENLYKENLDK
==========
Sequence: AnrP829849

AEFIKGATGVFGSGWFWLVYNTK
AYEWALK
DTEFAGKDLVSIIK
EFGSLENFK
EFGSLENFKAEFIK
EGMGSVSFYANELHPVK
FYAHINWEFVAK
HHNTYVTNLNNLIK
HHNTYVTNLNNLIKDTEFAGK
KLPYDTNAFGDFLSAETFSYHHGK
LEFVGTSNAATPITEDK
LPYDTNAFGDFLSAETFSYHHGK
NARPAYLEK
NQKLEFVGTSNAATPITEDK
==========
Sequence: AnrP550554

AEFKGEIVMR

AWAKGVLENLATNPK
DFGTFKEDQIPVSK
DVEVGNSLGIIFPNQDNR
EAVKIYDEVGFR
FAVMNTYYIGLLK
FMEFMLSPEIQK
GEIVMRSATAPYSK
GGDRDQAR
GTHINISGIAMTK
GTHINISGIAMTKSSK
GVLENLATNPK
GVLENLATNPKGGDR
HYNADFEIIK
HYNADFEIIKK
IAENIKEAVK
IIAYNKNTNIDISK
ILTDSNYEFPIR
ILTDSNYEFPIRNDVELSQTVK
IYDEVGFR
KFMEFMLSPEIQK
LSLEGSNSPADIFITADISNLTEAK
MKNYEDLAK
NDVELSQTVK
NLGLLSPVSSK
NPKDVEVGNSLGIIFPNQDNR
NTNIDISKMK
NYEDLAKAEFK
QVFAGEAK
RLSLEGSNSPADIFITADISNLTEAK
SSKNQDAAK
TGIKVNHTQAK
TLLASIIANDGNK
TLLASIIANDGNKEAK
VNHTQAKASELIK
YLEEFIPAHLR

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Sequence: AnrP139712

AAFNTFSEK
AAFNTFSEKEIEELK
AENYVLEIGSK
AFEGGKAENYVLEIGSK
AKQLDSVNATASVK
ALKEGDFAK
ASVEVLDEK
ASVEVLDEKLK
DGEIIAELILSFKPEIK
DIKVTFPK
DSFKEEAQK
EEAQKSVK
EHLENYK
EHLENYKK
ELTQDAEQNLFK
ELVGEPYFEK
ELVGEPYFEKFDR
ENKELVGEPYFEK
EYGAAHLAGK
EYGAAHLAGKDAVFK
FADALIEK

FADALIEKYNFDLPK
FATPEAIK
FATPEAIKTK
FDFEGFVDDK
FDFEGFVDDKAFEGGK
GIVEQETDMQMR
IEVNDQELIQAIYFEAYR
IGEEKDIK
IPELDDEMLK
IPELDDEMLKK
IPSGMIKSEVENLAK
KDGEIIAELILSFKPEIK
KIEVNDQELIQAIYFEAYR
KLLPGEEK
KQGALPAVK
LEGYEKLIPEYQTPK
LFNDIFIPK
LHEIQELK
LHEIQELKIPELDDEMLK
LIPEYQTPK
LLPGEEKASVEVLDEK
LTFIIDELAK
LTFIIDELAKLR
LVNDELKGK
MALIEEK
MDGFRPGK
MDGFRPGKVPVSAVLK
QFIPGFEDGMVGMK
QLDSVNATASVK
RFATPEAIK
SAVNSALQELKK
SEVENLAK
SVKMDGFRPGK
VPVSAVLKR
YERELTQDAEQNLFK
YGMNPKEHLENYK
YNFDLPK
==========
Sequence: AnrP602342

DENILTILK
DKGMIYGIGK
GETNGTGVGGNAGFVIDR
GETNGTGVGGNAGFVIDRLTEAIK
GMIYGIGK
GMIYGIGKR
GNVMPLIDLAQR
IDPPPETLVK
MTPQTRYIVLR
NRIDPPPETLVK
QQTQMAGPDVDQR
RDENILTILK
SNEKLEQILQK
VPSVPDYVLGVFNMR
==========
Sequence: AnrP467527

DIEPATFSTGSGALDK
DIEPATFSTGSGALDKGK

DIPIVFNSSLSNEFMNEK
EDPRFK
EMMQQMGFQVVEAK
FDENIVK
FKDIPIVFNSSLSNEFMNEK
FNASDFFNEIAK
FTGTALILDDSMTAR
GVQEAGGEGYLVK
GVVIPVVNLAK
IFKQGHDK
IIVSDVEMPQMDGFHFAAR
IPSLTELPGVPDYIEGIFDLR
KHQSQEQG
MFDENIVK
QGHDKVYEGIYGVNVSK
TDIDFGKIEK
TGSNEMELVDFR
VIITEFSNILIGFIVHEAKR
VKEMMQQMGFQVVEAK
VYEGIYGVNVSK
==========
Sequence: AnrP311344

AIYDDKNALIKPK
AMSEVKDEFLK
AVIIDAKYFSPLEQSYVITK
DKIVLGENISVPVLHVDSK
EFDLFFSADTK
EVLENLGLNELLK
EVLENLGLNELLKDK
ITHLSIANPK
IVLGENISVPVLHVDSK
KLAFEFNEFIGSSK
LAFEFNEFIGSSK
NSDIAIVAYSLVSSINHPK
QGREFDLFFSADTK
THPEDKIELVFGASGK
VAPYGVAAK
YFSPLEQSYVITK
==========
Sequence: AnrP505685

ALDFTAPAVLGNNEIVQDFNLYK
ALDFTAPAVLGNNEIVQDFNLYKNIGPK
ANPKGVAEYLGK
DFTFVCPSEIIAFDK
DFTFVCPSEIIAFDKR
FPLVADLTK
FPLVADLTKQIAR
GAVVFFYPK
GDEGMKANPK
GIEVIGISGDNEFSHFAWK
GSFLLDADGTVR
GSFLLDADGTVRHAVVNDLPLGR
GVAEYLGK
GVAEYLGKNEAK
HAVVNDLPLGR
KALDFTAPAVLGNNEIVQDFNLYK
MVDTMLFTNEHGEVCPAGWNK

NFDVLYAEAVALR
NFDVLYAEAVALRGSFLLDADGTVR
NIDEMLR
NIDEMLRMVDTMLFTNEHGEVCPAGWNK
NIGPKGAVVFFYPK
NTPVNQGGIGQVK
NTPVNQGGIGQVKFPLVADLTK
QIARNFDVLYAEAVALR
RYQEFK
YQEFKNR

==========

Sequence: AnrP681041

AGTLADQAK
ALTKEEQK
ASEFTLEK
ASEFTLEKAELGK
DQKGVDEILK
EAKSIETFLK
EMGSVQLGIK
FANLGDFK
FANLGDFKGDANGMVK
FDKFLEGDEK
FLEGDEKALTK
GDANGMVKTPTLR
GPIQADPEMATPAK
GVDEILKQNGVK
ISSLPEYVSEFK
ISSLPEYVSEFKK
KLYFEPR
NSGLVALPK
NSGLVALPKDQK
SGIISCNTCHNVGLGGTDGISTAIGHK
SGVNFDNIADAIANFER
SLTGTKPAIVYPQLPISTEK
TLITPSRFDK

==========

Sequence: AnrP72219

AGLNVLSLER
AITVGGQGASLPHK
ALHKFITDK
ALNYNFTR
AMSTGKYTIR
ASPLNTVIPK
ASPLNTVIPKAMSTGK
CAEGILKYHK
DAFGMPLLR
DAFGMPLLRLTYNFTDQDR
DMEPYYDR
DMEPYYDRFEK
DTVTFRHDPSGLALPYR
DYSVVPYQSTHNTGGTTMGADR
FEKTCGVSGEPNPLAEK
FGCEYGAK
FITDKTAEVAK
FMPYDFEIQTLSK
FVDTRTMK
GGYTNPDGQDLAPCQYCAYCER

GHMQSTENFNYIHDEWR
HDPSGLALPYR
HDPSGLALPYRK
KALNYNFTR
LLMVSNIGEQYDPK
LLMVSNIGEQYDPKTGK
LTYNFTDQDR
LTYNFTDQDRALHK
MGAFRSSPYPQEPLENTK
MQGVKSIK
NNYLSLDPTYK
SSNLHTYR
SSNLHTYRLPASNSK
SSPYPQEPLENTK
SSPYPQEPLENTKMLK
TCGVSGEPNPLAEK
TCGVSGEPNPLAEKMGAFR
TYSNVTQILK
TYSNVTQILKK
VTGVKFVDTR
YGINYGLMQDCSK
YGINYGLMQDCSKDTVTFR
YGNKLGNDYTLQDWGVTYK

==========

Sequence: AnrP490750

AHTDVGFK
AHTDVGFKIK
DIVLDAEIGGVAKGK
DNHLQQDDFFK
DNHLQQDDFFKAK
DYSAVIDFDPASAEFK
DYSAVIDFDPASAEFKK
EKIGFSLNGK
EYTLDKAHTDVGFK
GKMTGTLTIAGVSK
GNFKDYSAVIDFDPASAEFK
HLQISNVK
HLQISNVKGNFK
IASVNTENQTR
IASVNTENQTRDNHLQQDDFFK
IGFSLNGKIK
IKHLQISNVK
LDVTIKIASVNTENQTR
MTGTLTIAGVSK
VLLSSLVAVSLLSTGLFAK
YPDMTFTMK
YPDMTFTMKK

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Sequence: AnrP569688

AEVISSYSK
AGEHGRGFAVVADEVR
ATTEVEMNINLLK
ATTEVEMNINLLKQNANEMYTQSEQVEK
CEVAENASLDLFNVFK
DITQHSIINK
DITQHSIINKCEVAENASLDLFNVFK
DVAGTLHR

DVSDQTNLLALNAAIEAAR
EIFSKSGK
EMLDESDH
ERFGQNK
FGQNKSFLK
FGSKINHSDLQK
FQSENLELK
FQSENLELKNK
FTHLVNEAHSTNSNAVGIASEAFVSLAK
GFAVVADEVR
GFAVVADEVRK
IEKFQSENLELK
INEPHEK
INEPHEKVHENMNNAITIANTEDISK
INHSDLQK
INHSDLQKLEEENK
ISIDSNAHIMSFSEK
ITSLEQAALESK
ITSLEQAALESKLK
LDHIAFK
LEEENKNLTHK
LGKWLASTGK
LKTDLLNVLLTGVLK
LNGYKEIFSK
NKITSLEQAALESK
NLTHKIEK
QLADHTSCR
QLADHTSCRLGK
QNANEMYTQSEQVEK
SFLKINEPHEK
SGKQLADHTSCR
SVDEITNVINLIK
SVDEITNVINLIKDVSDQTNLLALNAAIEAAR
TDLLNVLLTGVLK
TQKATTEVEMNINLLK
TRDVAGTLHR
VHENMNNAITIANTEDISK
VHENMNNAITIANTEDISKDITQHSIINK
WLASTGKER

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Sequence: AnrP852550

DAEEGRTSLSSMEISTLK
DAHFDKLFDR
DELSQYLANYK
DELSQYLANYKK
ELMSELK
ELMSELKGK
GKDAHFDK
HNELDDMIK
HNELDDMIKDAEEGR
LFDRHNELDDMIK
LHEYRELMSELK
LHVKDELSQYLANYK
MLHEYR
MLHEYRELMSELK
TSLSSMEISTLK
TSLSSMEISTLKK

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Sequence: AnrP255677

AGIKSGDIILK
DFNDMKIQTNGEFGGLGITVGMK
DGALTVVSPIEGTPADK
DGALTVVSPIEGTPADKAGIK
DNKNLISQK
EDKQENK
EEQVQKR
EIIKIESVYAK
GATKPFDVTLTR
GATKPFDVTLTREIIK
GRIASENQEYK
GSVQQIIPINK
GSVQQIIPINKTEALR
GVIVGENTFGK
GVIVGENTFGKGSVQQIIPINK
IASENQEYK
IASENQEYKADPK
INDEATLGINLNDAVDK
INDEATLGINLNDAVDKMR
IQTNGEFGGLGITVGMK
KGATKPFDVTLTR
LEALDKLTK
MIENENILYLR
MMELILK
NNPGGLLNQAIGLVNLFVDK
QENKDNK
QHLESELEK
QHLESELEKIDK
QINDDAQLK
QINDDAQLKSAIDTIK
RGVIVGENTFGK
RLEALDK
SLSGLLSNLDAHSSFLNEK
TIQAVGVKPDIEVFPGK
TQITLTIFR
TQITLTIFRK
VNTQEDGFSIK
VNTQEDGFSIKESDLK
VTNFDKNVVDVASK
YPNVKGVILDLR
YYLPSGR

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Sequence: AnrP252410

AKVNFTDGTSDIYDR
AYKGCEGTNHGHVPFEDGTK
CGINVDDK
CGINVDDKGVPLMDENK
DIHEAGNSGK
DIHEAGNSGKVELK
EFTRLNDINLK
EHNIEVEFGSEVESVK
EHNIEVEFGSEVESVKNENGVFLVSTAK
ESTIETFQNALK
EVLILEK
EVLILEKSNNICQTLMQFYK
GCEGTNHGHVPFEDGTK

GCEGTNHGHVPFEDGTKESTIETFQNALK
GIFVAGDIATK
GVPLMDENK
GVPLMDENKQSNVK
GVYECKNIIVAIGR
IDLIVVGAGPTGIGCAVEAK
IDLIVVGAGPTGIGCAVEAKLK
IINFNANSVLGNEK
IIYAIGGSTPLDFLQK
ILVVGGGNSAAEYAVDLANSNQVSLCYR
KIDLIVVGAGPTGIGCAVEAK
LGIDINEVEDDNGK
LGIDINEVEDDNGKAK
LNDINLKDIHEAGNSGK
MGKPNKPDYK
NENGVFLVSTAK
NGASIVTGLNDAVK
NGASIVTGLNDAVKILSVL
NIIVAIGR
NIIVAIGRMGKPNKPDYK
NKEVLILEK
SNNICQTLMQFYK
SNNICQTLMQFYKDGK
VNFTDGTSDIYDR
==========
Sequence: AnrP916533

DTIEELVMSDVSK
ELFLALAK
IAGSSTVYPFTSFVAEEYASIK
IGLVPLSDDKLK
ILNDELVK
INAANIDGVTPSEESIADEK
INAANIDGVTPSEESIADEKYELAR
IPEYKGEYK
ISVYGPPSSSGTR
IYMSDDLAK
KELFLALAK
KILNDELVK
KISVYGPPSSSGTR
LIPNPYTNWNQINK
LSEFETCK
LSEFETCKK
QDGAYIPSGENDNLIVSK
TIRQDGAYIPSGENDNLIVSK
TNAPLNITK
TNAPLNITKK
TPIVESLGTGGGFK
VFCEGTTDISNASRPMK
==========
Sequence: AnrP126795

AGQSEEFAEISK
AGQSEEFAEISKCR
EFLKQNLK
FFILQKNLK
IGFDLEKSYK
IGGELVYSTCTFTK
ILLDAPCSTFAK

ILPSLDYDGFFIAK
INVYCYLFDAK
INVYCYLFDAKDK
KINVYCYLFDAK
LELLDIDLENVEAK
MQNILSSFAQEK
MQNILSSFAQEKNVCVFANTLK
NIGNLCPLK
NIGNLCPLKFDK
NLKNYGVNAK
NVCVFANTLKTSIEELEK
QNILSSFAQEK
SEFKLELLDIDLENVEAK
TSIEELEKEFLK

==========

Sequence: AnrP327756

DAELKIEK
DRMSVYDK
EANALKIEEDIAK
ELEEEKIK
EQLDAANDEIVR
EQLDAANDEIVRLDK
GEEIVTCPHCGR
GEEIVTCPHCGRILYK
IDEEIKDIENQK
IDQEIDSYEPK
IDQEIDSYEPKIDSINK
IDSINKTLK
IEEDIAKEQLDAANDEIVR
IEKINADLEK
IKQEQNINEIR
ILENKETYK
ILYKEQEEQN
IQNNAHISEFSAK
IYDKTYLSVVK
KELEEEK
KQACYGCFMK
LDKILENK
LVSEMNQK
MNKYLEQLVLLSK
MSVYDKK
NKYLEQLVLLSK
NTAVVPVKK
QACYGCFMK
QEQNINEIR
QEQNINEIRVSIK
SEMEVLEK
SEMEVLEKDR
SGVVKTEK
TEKEANALK
TKLVSEMNQK
TLKDAELK
TYLSVVKGEEIVTCPHCGR
VLSFYEK
VLSFYEKIR
VSIKSEMEVLEK
WAKNTAVVPVK
YLEQLVLLSK

==========

Sequence: AnrP684299

AENRAFGIYK
AFGIYKLK
DQKHYHVPITLSPFGYSTYR
DYYTSHK
FFTKDYYTSHK
HYHVPITLSPFGYSTYR
IGDLLPYEK
IGDLLPYEKAENR
INTFYPFVEVSFELSK
KVSEEFTEENGR
LEANQQWK
LEANQQWKK
VKVELYK
VSEEFTEENGR
VSEEFTEENGRIGDLLPYEK

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Sequence: AnrP586832

AFNKDLNK
AKFEGMIDSLVAETITK
ALDDLRETLK
ALSEVSHK
ALSEVSHKLAENMYK
ATKEAGTIAGLNVLR
DAELHKEEDK
DDDVIDAEVE
DEIKEIVMVGGSTR
DEPNTANDK
DEPNTANDKK
DETGIDLK
DETGIDLKNDVMALQR
DNKSLGNFNLEGIPPAPR
DVLLLDVTPLSLGIETLGGVMTK
EAGTIAGLNVLR
EAGTIAGLNVLRIINEPTSAALAYGLDK
EAVDARNAADSLAHQVEK
EEIESKMK
EFSRDNK
EGKNTTPSVVAFTDK
EIVMVGGSTR
EIVMVGGSTRVPLVQEEVK
ELSSANETEINLPFITADASGPK
ENIQKALDDLR
EQVFSTAEDNQSAVTINVLQGER
EQVFSTAEDNQSAVTINVLQGEREFSR
FEGMIDSLVAETITK
GDVKDVLLLDVTPLSLGIETLGGVMTK
GESKVIPNK
GEVLVGDSAK
GEVLVGDSAKR
GMPQIEVTFDIDANGILTVSAK
GTTIPTKK
IINEPTSAALAYGLDK
IINEPTSAALAYGLDKK
IMGLMINEDAAK
IMGLMINEDAAKEAK

INEVVSDAGLK
INEVVSDAGLKK
ITGSSGLSEEEINNMVK
ITGSSGLSEEEINNMVKDAELHK
IYTPQEISAK
KELSSANETEINLPFITADASGPK
KEQVFSTAEDNQSAVTINVLQGER
LAENMYK
LAENMYKK
LIDFLANEFK
LIDFLANEFKDETGIDLK
LKEAAENAK
LPYHITER
LPYHITERNGACAIEIAGK
MKALSEVSHK
MSKVIGIDLGTTNSCVAVYER
NAADSLAHQVEK
NAADSLAHQVEKSLSELGEK
NDVMALQR
NDVMALQRLK
NGACAIEIAGK
NGACAIEIAGKIYTPQEISAK
NQNASKEEIESK
NRLPYHITER
NTTPSVVAFTDK
NTTPSVVAFTDKGEVLVGDSAK
QAVTNPEK
RIMGLMINEDAAK
RQAVTNPEK
SKVIGIDLGTTNSCVAVYER
SLGNFNLEGIPPAPR
SLSELGEK
SLSELGEKVAAADK
SVNPDEVVAIGAAIQGAVIK
TIYSIKR
VAAADKENIQK
VIGIDLGTTNSCVAVYER
VIGIDLGTTNSCVAVYERGESK
VIPNKEGK
VPLVQEEVK
VPLVQEEVKK

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Sequence: AnrP524051

AIINEHYK
AIINEHYKDILIPAF
AKLIELNK
ALDDVDIAIINSNFALGAGLNPSK
ALEEKELDANLYQHKPFLEEYNLK
ALELLEKAK
DTIFREDK
EDKNSPYVNYVVVR
ELDANLYQHKPFLEEYNLK
ELDANLYQHKPFLEEYNLKK
FKAIINEHYK
GSNLIATTPVLIAPVGVYSK
GSNLIATTPVLIAPVGVYSKK
IKNLENLK
IVEFSDYILPNR

LIELNKNTLK
LKFIELK
NKGYELK
NLENLKEGAR
NSPYVNYVVVR
NTLKTPLDINK
TKVIDEILR
TPLDINKNPK
VAIPNDATNESR
VIDEILR

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Sequence: AnrP579672

ALDIIAKK
ALKTPLDIIDNPK
ALNDVDFAVINSNYALSANLNPAK
DSVFIEDK
DSVFIEDKESPYANILVVR
EGVKIAIPNDPTNESR
ESPYANILVVR
FVELKPAQLPR
IAIPNDPTNESR
IKFVELKPAQLPR
IKQFIIEK
QFIIEKYNGSVLPAF
QGYKLEIK
SLDDIKEGVK
TPLDIIDNPK
TPLDIIDNPKK
VAAIHIEPMAVYSK
VAAIHIEPMAVYSKK
VGHENDPK
VGHENDPKIK
YKSLDDIK
YNGSVLPAF

==========

Sequence: AnrP191193

AKDLSVIEIGAAGK
AVFVIKEGK
DLSVIEIGAAGK
EFGEKYGVLINEGALEGLLAR
ELVNEITEMPDIAK
FCSTEGIENLSVASDFVAK
FCSTEGIENLSVASDFVAKEFGEK
GNSVEVGADAPK
KVASYNGAEVIVVSMDLPFAMGR
LDAFFGGSSCCGGCGCH
LKGNSVEVGADAPK
MSIVNFK
SIVNFKGNPVK
TQIILSVPSLDTPVCATEAR
TQIILSVPSLDTPVCATEAREFNK
VASYNGAEVIVVSMDLPFAMGR
VAYKELVNEITEMPDIAK
YGVLINEGALEGLLAR

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Sequence: AnrP694298

AKEILSEFQR
CIHCYNHHK
DASYSDSLSHK
DASYSDSLSHKLADVYFVSYFLNK
DEQNGKDASYSDSLSHK
EAFPNLHFK
EILSEFQR
EILSEFQRANDIAK
LADVYFVSYFLNK
LADVYFVSYFLNKQR
LREAFPNLHFK
LYPVSLMNGEFSK
LYPVSLMNGEFSKEMNELFTFAQYK
MRNFFCK
NFSNLDEFYDIGLK
QRNFSNLDEFYDIGLK
TYGTPAFVVNGK
YQINPSAINSMQDLEDLVK

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Sequence: AnrP318705

AHSSTELK
DTKVNLDLK
KPIIKDTK
MMMQKIPEIIIK
NIDSKEF
SDISEVSELHTHIHK
SDISEVSELHTHIHKDGK
SGGYHIMLLK
SGGYHIMLLKLK
VNLDLKFNNHK

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Sequence: AnrP493933

ALFLSSNDLQLSR
ALLCFLDNQR
ALLCFLDNQRGR
AMSVANKDAILLHCLPAYR
DAILLHCLPAYR
DKDVVITDTWVSMGEENEK
DTARVIGAMVDFVMMR
DVVITDTWVSMGEENEK
DVVITDTWVSMGEENEKER
EEILSLVNHASELK
EEILSLVNHASELKK
EFEGFMIDEK
EWNKMQNGIAK
FEALKDK
GEPVKDTAR
GYEVSEEIFEK
HADVIFEEAR
HETLLEFAR
HETLLEFARYSK
HFLTLRDFSK
IKEFEGFMIDEK
ISLGYDKFEALK
ISPEIWEFAMK

ISPEIWEFAMKQALISGAK
KHFLTLR
LLQDKTLAMIFEK
LYVVKALLCFLDNQR
MAFELAITELGGK
MKHFLTLR
NRLYVVK
NYKISPEIWEFAMK
QALISGAKISLGYDK
TLAMIFEK
TLAMIFEKNSTR
TRMAFELAITELGGK
VIGAMVDFVMMR
VIGAMVDFVMMRVNK
VNKHETLLEFAR
==========
Sequence: AnrP979073

ATIKPSNAFMGEGNDIITNNITK
DMIGTKGEFK
DNKFEAK
GEFKNVEYK
GQLDLHTFK
GVISAKITMDK
ISFEGYK
KSTIVPLTYTIK
NIKDLASYLK
NVEYKFSK
STIVPLTYTIK
STIVPLTYTIKDNK
TKDMIGTK
VFFPALLGDTDIK
VVFQDVIAGENK
VVFQDVIAGENKGVISAK
==========
Sequence: AnrP257863

EFISVYEK
GDKLESSSGANR
IGVVLPLSGATAAYGQSALEGIK
IPLIAPAATGDR
LANSMQSALSNGDK
LANSMQSALSNGDKVSLAIIDTK
LSKEFISVYEK
NYQGVSGVISIDQTGNATR
QNYKDIINP
QYKSNGGQILR
SAVIVVDQSTDYSLGLAK
SLNPEFIFLPLYYSEASLFAR
SNGGQILR
SVVVKEIK
VAEDNKIPLIAPAATGDR
VCFMDSFQGSSLAK
VIGLIGEMVTANTLQVMR
VNSGDKDFR
VSLAIIDTK
VSLAIIDTKGDK
==========

Sequence: AnrP326257

AFENSFK
AFENSFKNNGGK
DFQAVGGVISIDESGNAIR
DFVAAYEK
EIQNQKQNYK
FATYVSKDLGLK
GDKLETSNGVNR
IHQTKDFQAVGGVISIDESGNAIR
IPLIAPVASGDK
KIPLIAPVASGDK
KLVINSGDK
LETSNGVNR
LSNGDVIKLITIDTK
LVINSGDK
LVINSGDKDFR
NAVIIIDQSNVYSLGLAR
NNGGKIIK
QNYKTIINP
SLNPDFVYMPIYHPEAALIAR
SVVIKEIQNQK
VCFKDSFQGDK
YASRVCFK

==========

Sequence: AnrP198268

DNDGFISK
EIFNLPIK
ELSIIKNEK
ESYDGIVPYK
FGGPNGLYLDR
FGGPNGLYLDRK
FLTHLNAPK
GAIFLNDIEK
IFKVELNK
LELPLMK
QYDELLK
SPESIFVDK
TKQYDELLK
TLYVVDIDVLR
YQEFDGFK
YQEFDGFKSPESIFVDK

==========

Sequence: AnrP515430

AEVITALK
AGVNNYIVKPFTPQVLK
EKLEDVLGTGSGEGAAE
IIKNTLTR
KYEDMPIIMVTTEGGK
LEDVLGTGSGEGAAE
LLVVDDSSTMR
LLVVDDSSTMRR
MKLLVVDDSSTMR
YEDMPIIMVTTEGGK

==========

Sequence: AnrP385049

AIEAHIETLK
CAVCHGANADK
CAVCHGANADKVYLNK
EYSEGKR
GLTEEDFK
GLTEEDFKAIEAHIETLK
KCAVCHGANADK
LLVVSALACLGVSAFAADGATLFKK
LNLKGLTEEDFK
LQYMKEYSEGK
NAYGQGAIMK
NAYGQGAIMKLNLK
RNAYGQGAIMK
VPALKTLSSAER
VYLNKVPALK

==========

Sequence: AnrP470247

DSDDIKLYSSGVVVQHFSNSQSIIAR
EFPQIYFTHIDIFGAQLIR.
GLVIAPDEQTYNELVR
LEFSVFSALK
LEFSVFSALKQDALPLPNVLPK
LYEVPISKPTSVQVPFYSR
LYSSGVVVQHFSNSQSIIAR
QDALPLPNVLPK
SELVKVDDIYGYIK
SNFFDFNSQEIGNYYR
TATLSPKR
VDDIYGYIK
VDDIYGYIKDSDDIK
VGDEVVLNFLYDR
YYDALINLPK
YYDALINLPKVQ

==========

Sequence: AnrP679791

ANRPSPLDDFFNDPYFK
AYKNQEGALITDVQK
DGENKQASFILK
DGYIVTNNHVVDDADTITVNLPGSDIEYK
DNIGLNQYENFIQTDASINPGNSGGALVDSR
DRLQIPK
DVNGVLVDSVK
DVNGVLVDSVKEK
ENPKGVQSDLIDGLSLR
GFLGVTILALQGDTK
GFLGVTILALQGDTKK
GGGNNGIGFAIPSNMVK
GKNSGFQEGDIIIGVGQSEIK
GSSADEAGLK
GSSADEAGLKR
GVQSDLIDGLSLR
GYLVGINSAILSR
IDRGFLGVTILALQGDTK
ISLSYER
ISLSYERDGENK

KSVVNISTSK
NGFATLLVLK
NLKDLEQALK
NQEGALITDVQK
NSGFQEGDIIIGVGQSEIK
NYIGTLEIGQK
QASFILKGEK
SPIDLKNYIGTLEIGQK
SVVNISTSK
VNPAAGNAVLSYHDSIK
VNPAAGNAVLSYHDSIKDAK
==========
Sequence: AnrP530915

AAVSTAVAAAAVK
AAVSTAVAAAAVKDGVAK
ALAPTVGGINLEDIAAPK
ANLVAIVSDGSAVLGLGNIGAQASKPVMEGK
AYFESLK
AYNLSTLEFGR
AYNLSTLEFGRDYVIPKPFDER
DNELAYTYTNK
DPVIFALANPIPEVMPEDVAR
DRNDLTPQK
DYVIPKPFDER
GADVFLGLSAPK
GALDVRASK
ILDDEMVLSMAK
KAYNLSTLEFGR
LEFAVDSK
LEFAVDSKEK
LPVSDAVKK
MNLKEEALK
NDLTPQKLEFAVDSK
NFDEKAYFESLK
NLGVENIILVDSK
NLKEEALK
SDYPNQINNVLGFPFIFR
TLKEVLK
VKNFDEK
VVVSGAGAAGIASAK
==========
Sequence: AnrP108083

AQFPNATVSVSNR
AQFPNATVSVSNRQK
AVAQKETMVIALGDK
DSLITPDLIDLK
EHLAQIDDELK
EHLAQIDDELKNYQVNYILTPVHGK
ETMVIALGDK
EVFSLYEK
NKPAIYVFSDPECPYCR
NYQVNYILTPVHGK
QENILFTK
SLGLSATPTIIK
TGISYAQEYEMK
TGISYAQEYEMKK
VGNTGFESVIVSVELNGQK

VSDAELKEVFSLYEK
YYDANIK
YYDANIKNYPK
==========
Sequence: AnrP947055

AQIELQTR
ASELTLLLK
ASFEALQK
ASFEALQKER
DAAIADVLSQMDAEDASK
EAEVNATLAK
EIYSQMK
EIYSQMKDAAIADVLSQMDAEDASK
ERLENLEK
IEELKLENAR
ILNSINDK
ILNSINDKTQGR
IMLSLESR
IMLSLESRK
ISGVLSKMDPK
KAQIELQTR
KASELTLLLK
QSLEAYK
VKEIYSQMK
==========
Sequence: AnrP407504

AEFRAFR
AFRDTINVRPNEELR
AIYKEELFLSPASR
ALPLLKNESK
ATLEIKENHIELIK
DALSHLKEK
DLMISDLR
DTINVRPNEELR
DTINVRPNEELRLK
EATTIHWHGVPVPPDQDGSPHDPILAGEER
EELFLSPASR
EELFLSPASRVEVLIDAPK
EESNTLFLANINLK
EFKEIIMSEDHMQMHGMMGK
EGEFVLINGQFKPK
EGEFVLINGQFKPKIK
EIIMSEDHMQMHGMMGK
EIIMSEDHMQMHGMMGKSENELK
EKDLMISDLR
EKLELPK
ENHIELIK
ENHIELIKGK
FEIPQDSAGTYWYHPHPHYTASK
FILVGTDGGLIEK
FILVGTDGGLIEKAIYK
IALASMFLINGK
IALASMFLINGKSYDLK
IDLSSKLGVVEDWIVINK
IEVFEGDK
IEVFEGDKLEILVK
IFKPLEEPK

IFKPLEEPKEFK
IKLATNER
IRIYNATAAR
IYNATAAR
IYNATAARYLNLR
IYRFEIPQDSAGTYWYHPHPHYTASK
KDALSHLK
KTLFYTYNGLVPAPK
LATNERIR
LDENAQIPNNNLNDWLNGR
LELPKNLK
LESAYYDR
LESAYYDRDK
LGVVEDWIVINK
LLDPKQFPQGEILK
MMVKEESNTLFLANINLK
MYHCHILEHEDLGMMGNLEVK
MYHCHILEHEDLGMMGNLEVKE
NFLKFNALTLASMGVAYANPMHDMHSMHK
NHSINHDLDTSFINFAPK
NHSINHDLDTSFINFAPKNLK
NIFRATLEIK
NLKIFKPLEEPK
NLKLLDPK
QDFKGLR
QFPQGEILK
QVFMGLAGAFVIK
QVFMGLAGAFVIKAK
SENELKIALASMFLINGK
SHMDHPFHIHGTQFELISSK
TLFYTYNGLVPAPK
TLFYTYNGLVPAPKIEVFEGDK
VEVLIDAPK
VEVLIDAPKDGNFK
VQKAEFR
YLNLRIQGAK

==========

Sequence: AnrP818860

AEKEFMK
ESLELIKNEK
GKPNLVIVNEGDDSLK
GKPNLVIVNEGDDSLKNFYSVIATNPK
GTYIKYEANEK
KGVILTDR
LLNKPLFVIDAK
LTFISRGDK
MATTTSTDNTGLLDALKPLYEK
MGEDCNADVLFVHSPK
NFYSVIATNPK
NLKESLELIK
NVNYTEASK
QSWYQQSGQGMLASIK
SGTDNKEK
TLNFIADFK
TPVMYNDFIIIADK
WVAVGTGAALK

==========

Sequence: AnrP355324

AEDLLVSAGFK
AEDLLVSAGFKK
ALMFNLDNEFLK
ALMFNLDNEFLKDLK
ANEHFYLDK
ANEHFYLDKVK
ARNTSNLEER
DDVLWHDGVKFSADDVK
DTLIIAVENEIAR
FDENMSLKPDLAK
FDENMSLKPDLAKSWDISK
FSIEAFK
FSIEAFKNPK
HIFDPSIASAELK
ILEFEIWAMSNDPLR
INPAYSEDHDAVINLVFSGLTR
IYKYDPK
KGEYVEFK
KVDIALQK
NDENFGILR
NDENFGILREK
NKDGNFEK
NLLHDYAFVANHPLER
NTSNLEER
QALNYAVDKESIVK
SVEILNPSHVK
TLGHHGVGFTWNVYEWSK
TPRLIIK
VDIALQKAR
VSLAGILQSEFR
VSLAGILQSEFRK
VVAKPAGSFDYSK

==========

Sequence: AnrP111949

AEDQIVGIATLQHSNIYPK
AERLEDITK
EKEAELLK
IIDRIQEFK
KLSDKPLNK
LSDKPLNK
LTSVGTFSNPSLEK
NITTLGQITK
NLSPQSQISRPVISAEYILK
NNLLDTNALLK
QNPDILILGINAK
SINLKAER

==========

Sequence: AnrP294550

ELNGMEIAAVYLQPIEMEPR
FKYTGTPK
GGFGVGNYELTFYISNPEK
GGFGVGNYELTFYISNPEKQGFGR
GIDLAASLADIHLEADIHALK
GTLMPMVADDGPHYGANIAMEK
GTLMPMVADDGPHYGANIAMEKDK

HVDEETGVGK
HVDEETGVGKWFEPFK
KGGFGVGNYELTFYISNPEK
NTDTGAIKR
QGFGRHVDEETGVGK
RGTLMPMVADDGPHYGANIAMEK
WFEPFK
WFEPFKVDYK
==========
Sequence: AnrP407676

ASMLNYEGMPAFALSENLLAVLK
DNMDLNISTEVFAK
ELQNILSAGNDFSILIER
FEDFLAGYER
FNLPDSKPKPK
FQFFIR
GSTLYFQVLRDNMDLNISTEVFAK
IGLLGTPCCEMMGIALNNSSFIGNR
IYVNNVR
LNEKILFADR
NDWVGIWDPNKPYIGHIK
NPQFLINDQVISVDGLPANDLR
NPQFLINDQVISVDGLPANDLRK
TDFSLIPTPMGDEEK
TDFSLIPTPMGDEEKLTR
YDPFLNLYLVR
YLAQNIDEK
YLAQNIDEKDQLDFNSK
YLKHFMK

Claims

1. A vaccine comprising a pharmaceutically-acceptable carrier and
   - a polypeptide comprising a sequence having at least 95% sequence identity to any of the sequences selected from the group of surface-located Campylobacter jejuni polypeptides of SEQ ID NO:1-51, or comprising an antigenic fragment of any of said sequences,
   - a polynucleotide comprising a sequence encoding said polypeptide,
   - an expression vector comprising a sequence encoding said polypeptide, or
   - a recombinant virus or recombinant cell comprising said polynucleotide or said expression vector.

2. The vaccine of claim 1, wherein the fragment comprises 6 or more consecutive amino acids of said sequence.

3. The vaccine of claim 1 or 2, wherein the fragment comprises less than 99%, such as less than 75%, e.g. less than 50%, such as less than 25%, e.g. less than 20%, such as less than 15%, or e.g. less than 10% of the full-length of said sequence.

4. The vaccine of any of claims 1-3, wherein the fragment comprises less than 70 consecutive amino acid residues, e.g. less than 50, such as less than 40, e.g. less than 30, such as less than consecutive 20 residues of said sequence.

5. The vaccine of any of claims 1-4, wherein the fragment comprises 6 or more, such as 7 or more, e.g. 8 or more, such as 9 or more, e.g. 10 or more consecutive amino acids of said sequence.

6. The vaccine of any of claims 1-5, wherein the fragment comprises one or more residues of any of the fragments of SEQ ID NO:52-119, e.g. two or more consecutive, such as three or more consecutive, e.g. four or more consecutive, such as 5 or more consecutive resides, e.g. 6 or more consecutive residues of any of the fragments of SEQ ID NO:52-119.

7. The vaccine of any of the preceding claims, wherein the polypeptide has at least 96%, e.g. at least 97%, such as at least 98%, e.g. at least 99%, such as 100% sequence identity to any of said sequences.

8. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:1, or an antigenic fragment thereof.

9. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:2, or an antigenic fragment thereof.

10. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:3, or an antigenic fragment thereof.

11. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:4, or an antigenic fragment thereof.

12. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:5, or an antigenic fragment thereof.

13. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:6, or an antigenic fragment thereof.

14. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:7, or an antigenic fragment thereof.

15. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:8, or an antigenic fragment thereof.

16. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:9, or an antigenic fragment thereof.

17. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:10, or an antigenic fragment thereof.

18. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:11, or an antigenic fragment thereof.

19. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:12, or an antigenic fragment thereof.

20. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:13, or an antigenic fragment thereof.

21. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:14, or an antigenic fragment thereof.

22. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:15, or an antigenic fragment thereof.

23. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:16, or an antigenic fragment thereof.

24. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:17, or an antigenic fragment thereof.

25. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:18, or an antigenic fragment thereof.

26. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:19, or an antigenic fragment thereof.

27. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:20 or an antigenic fragment thereof.

28. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:21, or an antigenic fragment thereof.

29. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:22, or an antigenic fragment thereof.

30. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:23, or an antigenic fragment thereof.

31. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:24, or an antigenic fragment thereof.

32. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:25, or an antigenic fragment thereof.

33. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:26, or an antigenic fragment thereof.

34. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:27, or an antigenic fragment thereof.

35. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:28, or an antigenic fragment thereof.

36. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:29, or an antigenic fragment thereof.

37. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:30, or an antigenic fragment thereof.

38. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:31, or an antigenic fragment thereof.

39. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:32, or an antigenic fragment thereof.

40. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:33, or an antigenic fragment thereof.

41. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:34, or an antigenic fragment thereof.

42. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:35, or an antigenic fragment thereof.

43. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:36, or an antigenic fragment thereof.

44. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:37, or an antigenic fragment thereof.

45. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:38, or an antigenic fragment thereof.

46. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:39, or an antigenic fragment thereof.

47. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:40, or an antigenic fragment thereof.

48. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:41, or an antigenic fragment thereof.

49. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:42, or an antigenic fragment thereof.

50. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:43, or an antigenic fragment thereof.

51. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:44, or an antigenic fragment thereof.

52. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:45, or an antigenic fragment thereof.

53. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:46, or an antigenic fragment thereof.

54. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:47, or an antigenic fragment thereof.

55. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:48, or an antigenic fragment thereof.

56. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:49, or an antigenic fragment thereof.

57. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:50, or an antigenic fragment thereof.

58. The vaccine of any of claims 1-7, wherein the polypeptide comprises SEQ ID NO:51, or an antigenic fragment thereof.

59. The vaccine of any of the preceding claims, wherein the vaccine further comprises an immunogenic carrier, such as a carrier protein, wherein the carrier is preferably bound, covalently or non-covalently, to said polypeptide.

60. The vaccine of any of the preceding claims, wherein the recombinant cell is an attenuated or reduced-virulence Escherichia coli or Salmonella cell.

61. The vaccine of any of claims 1-60, wherein the recombinant cell is alive.

62. The vaccine of any of claims 1-60, wherein the recombinant cell is dead.

63. The vaccine of any of the preceding claims, further comprising an adjuvant.

64. The vaccine of any of the preceding claims, wherein the vaccine is suitable for systemic administration.

65. The vaccine of any of the claims 1-63, wherein the vaccine is suitable for intravenous, intramuscular, or subcutaneous administration.

66. The vaccine of any of the claims 1-63, wherein the vaccine is suitable for oral administration.

67. The vaccine of any of the claims 1-63, wherein the vaccine is suitable for intranasal administration.

68. An antibody capable of specifically binding any of the polypeptides of SEQ ID NO:1-36 or a fragment thereof.

69. The antibody of claim 68, wherein the antibody furthermore is capable of specifically binding an intact Campylobacter jejuni cell.

70. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:1, or a fragment thereof.

71. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:2, or a fragment thereof.

72. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:3, or a fragment thereof.

73. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:4, or a fragment thereof.

74. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:5, or a fragment thereof.

75. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:6, or a fragment thereof.

76. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:7, or a fragment thereof.

77. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:8, or a fragment thereof.

78. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:9, or a fragment thereof.

79. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:10, or a fragment thereof.

80. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:11, or a fragment thereof.

81. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:12, or a fragment thereof.

82. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:13, or a fragment thereof.

83. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:14, or a fragment thereof.

84. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:15, or a fragment thereof.

85. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:16, or a fragment thereof.

86. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:17, or a fragment thereof.

87. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:18, or a fragment thereof.

88. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:19, or a fragment thereof.

89. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:20, or a fragment thereof.

90. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:21, or a fragment thereof.

91. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:22, or a fragment thereof.

92. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:23, or a fragment thereof.

93. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:24, or a fragment thereof.

94. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:25, or a fragment thereof.

95. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:26, or a fragment thereof.

96. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:27, or a fragment thereof.

97. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:28, or a fragment thereof.

98. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:29, or a fragment thereof.

99. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:30, or a fragment thereof.

100. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:31, or a fragment thereof.

101. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:32, or a fragment thereof.

102. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:33, or a fragment thereof.

103. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:34, or a fragment thereof.

104. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:35, or a fragment thereof.

105. The antibody of any of claims 68-69, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:36, or a fragment thereof.

106. An antibody capable of specifically binding any of the polypeptides of SEQ ID NO:37-51 and capable of specifically binding an intact Campylobacter jejuni cell.

107. The antibody of claim 106, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:37, or a fragment thereof.

108. The antibody of claim 106, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:38, or a fragment thereof.

109. The antibody of claim 106, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:39, or a fragment thereof.

110. The antibody of claim 106, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:40, or a fragment thereof.

111. The antibody of claim 106, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:41, or a fragment thereof.

112. The antibody of claim 106, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:42, or a fragment thereof.

113. The antibody of claim 106, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:43, or a fragment thereof.

114. The antibody of claim 106, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:44, or a fragment thereof.

115. The antibody of claim 106, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:45, or a fragment thereof.

116. The antibody of claim 106, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:46, or a fragment thereof.

117. The antibody of claim 106, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:47, or a fragment thereof.

118. The antibody of claim 106, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:48, or a fragment thereof.

119. The antibody of claim 106, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:50, or a fragment thereof.

120. The antibody of claim 106, wherein the antibody is capable of specifically binding the polypeptide of SEQ ID NO:51, or a fragment thereof.

121. The antibody of any of claims 68 to 120, wherein the antibody is polyclonal.

122. The antibody of any of claims 68 to 120, wherein the antibody is monoclonal.

123. The antibody of claim 121 or 122, wherein the antibody is a human or humanised antibody.

124. The antibody of claim 123, wherein the antibody is a human antibody.

125. The antibody of any of claims 68-124, wherein the antibody is a binding fragment of an antibody.

126. The antibody of any of claims 68-125, wherein the antibody has a dissociation constant or Kd less than 5×10^{-6}M, such as less than 10^{-6}M, e.g. less than 5×10^{-7}M, such as less than 10^{-7}M, e.g. less than 5×10^{-8}M, such as less than 10^{-8}M, e.g. less than 5×10^{-9}M, such as less than 10^{-9}M, e.g. less than 5×10^{-10}M, such as less than 10^{-10}M, e.g. less than 5×10^{-11}M, such as less than 10^{-11}M, e.g. less than 5×10^{-12}M, such as less than 10^{-12}M, e.g. less than 5×10^{-13}M, such as less than 10^{-13}M, e.g. less than 5×10^{-14}M, such as less than 10^{-14}M, e.g. less than 5×10^{-15}M, or less than 10^{-15}M.

127. A pharmaceutical composition comprising a pharmaceutically-acceptable carrier and

- an isolated polypeptide which comprises any of the sequences of SEQ ID NO:1-36, or comprises a fragment or variant of any of said sequences,
- an isolated polynucleotide comprising a sequence encoding said polypeptide,
- an expression vector comprising a sequence encoding said polypeptide, or
- a recombinant virus or recombinant cell comprising said polynucleotide or said expression vector.

128. A pharmaceutical composition comprising an antibody as defined in any of claims 68-126 and a pharmaceutically-acceptable carrier.

129. A fragment of any of the polypeptides of SEQ ID NO:1-51, wherein the fragment is antigenic.

130. The fragment of claim 129, wherein the fragment is surface-exposed.

131. The fragment of claim 129 or 130, wherein the fragment is capable of inducing antibodies that can specifically bind an intact Campylobacter jejuni cell.

132. The fragment of any of claims 129-131, wherein the fragment comprises one or more residues of any of the fragments of SEQ ID NO:52-119, e.g. two or more consecutive, such as three or more consecutive, e.g. four or more consecutive, such as 5 or more consecutive resides, e.g. 6 or more consecutive residues of any of the fragments of SEQ ID NO:52-119.

133. An isolated polynucleotide comprising a sequence encoding the antigenic fragment of any of claims 129-132, wherein said polynucleotide does not comprise a sequence encoding the full-length polypeptide of any of SEQ ID NO:1-51.

134. An expression vector suitable for DNA vaccination comprising a sequence encoding a polypeptide which comprises any of the sequences of SEQ ID NO:1-51, or comprises a fragment or variant of any of said sequences.

135. An expression vector comprising a polynucleotide sequence encoding a polypeptide which comprises any of the sequences of SEQ ID NO:1-36, or comprises an antigenic fragment or variant of any of said sequences, said polynucleotide sequence being under the control of a promoter that directs expression of the sequence in Escherichia coli or Salmonella.

136. A recombinant cell transformed or transfected with a polynucleotide comprising a sequence encoding a polypeptide, said polypeptide comprising any of the sequences of SEQ ID NO:1-36, or comprising an antigenic fragment or variant of any of said sequences.

137. The recombinant cell of claim 136, wherein the recombinant host cell is an Escherichia coli or Salmonella cell.

138. The recombinant cell of claim 136 or 137, wherein recombinant the cell is an attenuated or reduced-virulence cell.

139. A recombinant attenuated or reduced-virulence Escherichia coli or Salmonella cell transformed or transfected with a polynucleotide comprising a sequence encoding a polypeptide, said polypeptide comprising any of the sequences of SEQ ID NO:37-51, or comprising an antigenic fragment or variant of any of said sequences.

140. A composition comprising a carrier and any one or more of
- an antibody as defined in any of claims 68-126,
- a fragment as defined in any of claims 129-132,
- a polynucleotide as defined in claim 133,
- an expression vector as defined in claim 134 or 135,
- a recombinant cell as defined in any of claims 136-138,
- an Escherichia coli or Salmonella cell as defined in claim 139,

141. Any one of the following
- a polypeptide which comprises any of the sequences of SEQ ID NO:1-51, or comprises a fragment or variant of any of said sequences,
- a polynucleotide comprising a sequence encoding said polypeptide,
- an expression vector comprising a sequence encoding said polypeptide,
- a recombinant virus or recombinant cell comprising said polynucleotide or said expression vector,
- an antibody capable of specifically binding said polypeptide,

or
- a composition as defined in claim 140,

for use as a medicament.

142. Use of
- a polypeptide which comprises any of the sequences of SEQ ID NO:1-51, or comprises a fragment or variant of any of said sequences,
- a polynucleotide comprising a sequence encoding said polypeptide,
- an expression vector comprising a sequence encoding said polypeptide,
- a recombinant virus or recombinant cell comprising said polynucleotide or said expression vector,

or

- a composition as defined in claim 140,

for the preparation of a medicament for the immunisation of an animal or human being against Campylobacter jejuni infections.

143. The use of claim 142, wherein the immunisation induces a protective immune response.

144. The use of claim 142 or 143, wherein the medicament is a medicament suitable for parenteral, intravenous, intramuscular, subcutaneous, oral or intranasal administration.

145. Use of an antibody as defined in any of claims 68-126, for the manufacture of a medicament for the treatment or prevention of Campylobacter jejuni infections in an animal or human being.

146. The use of any of claims 142-145, wherein the animal is a chicken, duck, turkey, cow or pig.

147. The use of any of claims 142-145, wherein the human being is in an at-risk population, such as the population of immunocompromised patients, the population of children up to 4 years old, the population of persons in industrialised nations or the population of naive or semi-immune travellers to the developing world.

148. A method for raising specific antibodies to a polypeptide of any of SEQ ID NO:1-36 in an (non-human) animal comprising the steps of

a. providing
   - a polypeptide comprising any of the sequences of SEQ ID NO:1-36, or comprising a fragment or variant thereof,
   - a polynucleotide comprising a sequence encoding said polypeptide,
   - an expression vector comprising a sequence encoding said polypeptide, or
   - a recombinant cell as defined in any of claims 136-138,
b. introducing a composition comprising said polypeptide, polynucleotide, vector or recombinant cell into said animal,

c. raising antibodies in said animal, and
d. isolating and optionally purifying the antibodies.

149. A method for raising specific antibodies to a polypeptide of any of SEQ ID NO:37-51 in an (non-human) animal wherein the antibodies are capable of specifically binding an intact Campylobacter jejuni cell, the method comprising the steps of

a. providing
   - a polypeptide comprising any of the sequences of SEQ ID NO:37-51, or comprising a fragment or variant thereof,
   - a polynucleotide comprising a sequence encoding said polypeptide,
   - an expression vector comprising a sequence encoding said polypeptide, or
   - a recombinant Escherichia coli or Salmonella cell as defined in claim 139,
b. introducing a composition comprising said polypeptide, polynucleotide, vector or recombinant cell into said animal,
c. raising antibodies in said animal,
d. isolating and optionally purifying the antibodies, and
e. selecting antibodies capable of specifically binding an intact Campylobacter jejuni cell.

150. The method of claim 148 or 149, wherein the raising of antibodies is done in a transgenic animal which can produce human antibodies.

151. A method for detecting Campylobacter jejuni comprising the steps of

a. providing a biological sample,
b. contacting said sample with an indicator moiety capable of specifically binding any of the polypeptides of SEQ ID NO:1-36, and
c. determining whether a signal has been generated by the indicator moiety.

152. The method of claim 151, wherein the indicator moiety furthermore is capable of specifically binding intact Campylobacter jejuni cells.

153. A method for detecting Campylobacter jejuni comprising the steps of

a. providing a biological sample,

b. contacting said sample with an indicator moiety capable of specifically binding any of the polypeptides of SEQ ID NO:37-51, wherein the indicator moiety furthermore is capable of specifically binding intact Campylobacter jejuni cells, and

c. determining whether a signal has been generated by the indicator moiety.

154. The method of any of claims 151-153, wherein said indicator moiety does not pass through the outer membrane of a Campylobacter jejuni cell.

155. The method of any of claims 151-154, wherein said indicator moiety is or comprises an antibody, such as an antibody as defined in any of claims 68-126.

156. A method for identifying a binding partner of any of the polypeptides of SEQ ID NO:1-36 or a fragment thereof, comprising the steps of

a. providing any of the polypeptides of SEQ ID NO:1-36 or a fragment thereof,

b. contacting said polypeptide or fragment with a putative binding partner, and

c. determining whether said putative binding partner is capable of binding to said polypeptide or fragment.

157. The method of claim 156, wherein the putative binding partner is a host-derived molecule.

158. The method of any of claims 156-157, wherein said method is repeated for a plurality of putative binding partners.

159. A method for identifying a compound with antibacterial activity against Campylobacter jejuni comprising the steps of

a. providing a sensitised cell which has a reduced level of any of the polypeptides of SEQ ID NO:1-36, and

b. determining the sensitivity of said cell to a putative antibacterial compound, for instance by a growth assay.

160. The method of claim 159, wherein said method is repeated for a plurality of putative antibacterial compounds.

161. The method of any of claim 159 or 160, wherein the putative antibacterial compound does not pass through the outer membrane of a Campylobacter jejuni cell.

162. A method for identifying a compound with antibacterial activity against Campylobacter jejuni comprising the steps of

a. providing a sensitised cell which has a reduced level of any of the polypeptides of SEQ ID NO:37-51, and

b. determining the sensitivity of said cell to a putative antibacterial compound, for instance by a growth assay, wherein the putative antibacterial compound is not capable of passing through the outer-membrane of a Campylobacter jejuni cell.

163. The method of claim 162, wherein said method is repeated for a plurality of putative antibacterial compounds.

164. A method for finding an inhibitor of any of the polypeptides of SEQ ID NO:1-36 comprising the steps of

a. providing two cells which differ in the level of any of the polypeptides of SEQ ID NO:1-36,

b. determining the sensitivity of said cells to a putative inhibitor, for instance by a growth assay, and

c. determining whether said two cells are differently affected by the presence of said putative inhibitor.

165. The method of claim 164, wherein the two cells differ in the copy number of said polypeptide.

166. The method of claim 164, wherein the two cells differ in the activity of said polypeptide.

167. The method of any of claims 164-166, wherein said method is repeated for a plurality of putative inhibitors.

168. The method of any of claims 164-167, wherein the putative binding partner does not pass through the outer membrane of a Campylobacter jejuni cell.

169. A method for finding an inhibitor of any of the polypeptides of SEQ ID NO:37-51 comprising the steps of

a. providing two cells which differ in the level of any of the polypeptides of SEQ ID NO:37-51,

b. determining the sensitivity of said cells to a putative inhibitor, for instance by a growth assay, wherein the putative inhibitor is not capable of passing through the outer membrane of a Campylobacter jejuni cell, and

c. determining whether said two cells are differently affected by the presence of said putative inhibitor.

170. The method of claim 169, wherein the two cells differ in the copy number of said polypeptide.

171. The method of claim 169, wherein the two cells differ in the activity of said polypeptide.

172. The method of any of claims 169-171, wherein said method is repeated for a plurality of putative inhibitors.

Figure 1

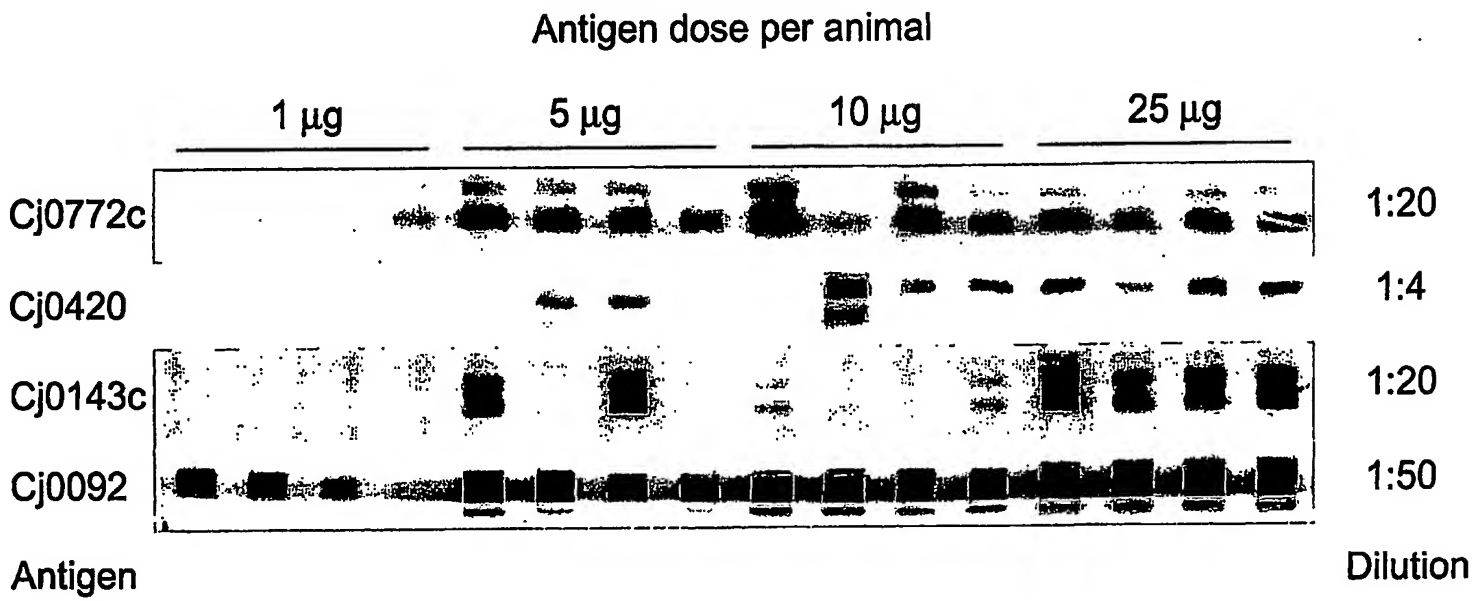

Antigen dose per animal
1 µg
5 µg
10 µg
25 µg
Cj0772c
Cj0420
Cj0143c
Cj0092
1:20
1:4
1:20
1:50
Antigen
Dilution

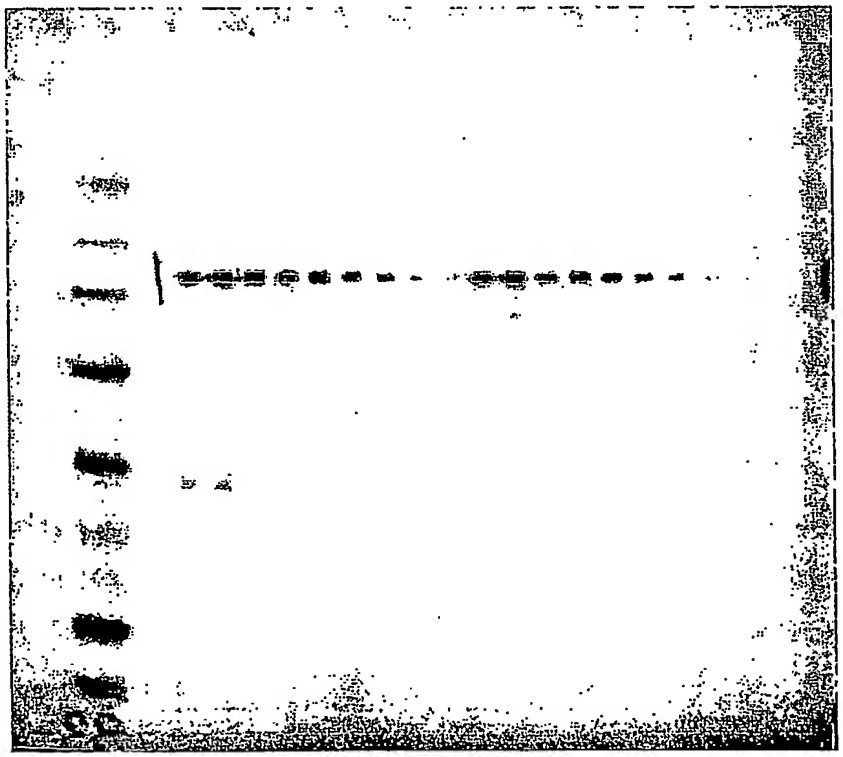
Figure 2

Titration of Antibody against Cj0092 (SEQ ID NO:1).

100ng of purified Cj0092 antigen was loaded on the gel, blotted and probed with different dilutions of mouse anti Cj0092 Antibody.
Dilutions are from left to right (for two individual animals): 1:50, 1:50, 1:100, 1:200, 1:400, 1:800, 1:1600, 1:3200, 1:6400

Lane 1: Marker proteins MW in kD: 97, 64, 51, 39, 28, 19, 14,

The antigen can be seen in all dilutions of the antibodies.



Sequence listing

SEQ ID NO:1
ACE83 Cj0092
>AnrP630851 (NC_002163) putative periplasmic protein [Campylobacter jejuni]
MKKILFIGSLVMASLLYAQGSQPVEITQQDINTQNEMSDASTKDITPKSIEDFFEEFADNFGIEYGITKD
GKTFYTGKSTVAVNDTDPQFAQALQNAYQKAMLNLQSEFIRDAFGRIATSKIQNYEADNSTNAKEFDELP
KGDKVDQILNKLTQLAGAQLDKALKDLGIDTNSLSEDRKKTLLKQEFLNKTMTNAIGSMSGLVPVQTIVT
QRRGEYDVGVVAVISNKTRQLAKDMALARQSAIKGKGKAISEYLPKDTKGFLNEYGIRLVYDENGAPIIL
SYGNWGYVADPSNAKKTNILEDRAKETALTMADAAIIEFINTNLSLKDERTTGDTYEEIIKQSINVNDSS
TQEQTQNITNIIDKVNSKIKASASGKIRGIRTLKKWSYTSENGIEHVGAVRFYSYENLANTNEALNSKSN
ATKNEAKKSSSIQRSSNVVNSMDDF

SEQ ID NO:2
ACE 5 Cj0005
>AnrP544820 (NC_002163) putative molybdenum containing oxidoreductase
[Campylobact
MKQNDQKENRRDFLKNIGLGLFGISVLSNFSFENFLGSKALAKELPDFKIEGKKDLIYHGEKPLTAETEI
YALDSDFTKPENFFVRNNGLPPSLETIKERLHKGWTLEIDGESIINKKSYTIEDLKKKFKTYTYALTVEC
GGNGRSEVIPSTKGTQWGYGAVACGRWTGVRLKDILKDCGIKNDAVYIGYYGIDTKLNGEETSPISRGVP
ISKALQDETLIAWAYEGKDIPLVNGYPLRLVCGGYPASTSGKWLYKISVRNKIHDGEKMEGSYKVPVNPV
KPGDFNYKGEMKIIESMPIRSVITNIKNGSEIKANKKFEVRGKAWAGELEVSEVYVSNDYGVTWTKAKVE
KPLNRLAWQKWSAQISIPTKGYYEIWARAIDSQGNSQPMVLAQWNPGGYINNACHRVNVYGV

SEQ ID NO:3
ACE 29 Cj0029
>AnrP372217 (NC_002163) cytoplasmic L-asparaginase [Campylobacter jejuni]
MKKAKSRIAILGTGGTIAGFIDSTIATTGYAAGAIDIDVLIKAVPQIRDLADISWEQIANIDSSNMCDEI
WLRLAKKIAKLFAEGIDGVVITHGTDTMEETAYFLNLTIKSDKPVVLVGAMRPSTAISADGPKNLYNAVA
LVVNKEAKNKGVMVAINDKILSARGVVKTHSLNVDAFSSPDFGDLGYIVDGKVFFYNNVIKAHTKNAPFD
VSKLTSLPKVDILYSYSNDGSGVAAKALFEHGTKGIVVAGSGAGSIHKNQKDVLKELLKKGLKVVVSSRV
VAGCVAVSDSDEKLGFISAEDLNPQKARVLLMLALTKTSDPKKIQEYFLKY

SEQ ID NO:4
ACE 37 Cj0037
>AnrP501075 (NC_002163) putative cytochrome c [Campylobacter jejuni]
MKKHILLLGLCLSLSLSAKSVSDYKVGEELSDKEGVEYFKELSKRPVQEWPNKNLSINDVPKGKQGDLIR
YGIELLSKTESTLGPYSKLKKTSNEVNCISCHMDNDGNGLPGTKKYVIPFLNILNNYPRLDIETMKIISV
EDRIRGMGGTDSHRFPNDSKEMKAILAYFKWLKEAYGIKDGVKLEGDFFAKMNFPNRPADPVRGKKLFEE
NCVACHGERGLGVKNDNYEQGSGHLYPSLLIYPDGGHMAMIPFLARFLKSAMPFGASADNPILSDEDALD
IAAYVNTGFVRMPITTTENRAGLDTAYSKSPSLKPEYFASPQQNLDPKEYIKVKYGPWKNPNHFPGE

SEQ ID NO:5
ACE 84 Cj0093
>AnrP666574 (NC_002163) putative periplasmic protein [Campylobacter jejuni]
MKIIKILFLGLFLSLSLNAKVITTTSTKSSTGEGTGLTREDAINNAIIEAIGKMSGVSINSLKKSNTSVS
TDNSGSNIQDNYSEQISKATKGRADTYEINSVEQDANGKYTANVTIFKTTTTKKYQAPGLSADNRRSITV
FDSTPDAAKRGIGSALQQKIISDLLQSRKFNVLDRDSSGYYEMEKALIKSGDAASDEVYKLKNMLATDYI
LLFSISGLEGKQKTSNLTGKSKTEIEVIVDYRVLLFATRQIKFSNTLSMKVNLKDNSLSANETALKQIAN
RIAGDILNAIYPLKVASVENNEVIFSQSLNQGDVYECFALGKVIKDTYTKENTGRVESKTGSIEITRTSP
KFSYAKITEGSVKVGDICRPLSNTGSGNGYTIGRDANYQTQEGGGVNLGF

SEQ ID NO:6
ACE 98 Cj0107
>AnrP732169 (NC_002163) ATP synthase F1 sector beta subunit [Campylobacter jejuni]
MQGFISQVLGPVVDVDFNDYLPQINEAIVVNFESEGKKHKLVLEVAAHLGDNRVRTIAMDMTDGLVRGLK
AEALGAPISVPVGEKVLGRIFNVTGDLIDEGEEISFDKKWAIHRDPPAFEDQSTKSEIFETGIKVVDLLA
PYAKGGKVGLFGGAGVGKTVIIMELIHNVAFKHSGYSVFAGVGERTREGNDLYNEMKESNVLDKVALCYG
QMNEPPGARNRIALTGLTMAEYFRDEMGLDVLMFIDNIFRFSQSGSEMSALLGRIPSAVGYQPTLASEMG
KFQERITSTKKGSITSVQAVYVPADDLTDPAPATVFAHLDATTVLNRAIAEKGIYPAVDPLDSTSRMLDP
NIIGEEHYKVARGVQSVLQKYKDLQDIIAILGMDELSEEDKLVVERARKIEKFLSQPFFVAEVFTGSPGK
YISLEDTIAGFKGILEGKYDHLPENAFYMVGNIDEAIAKADKLKG

SEQ ID NO:7
ACE 103 Cj0112
>AnrP511634 (NC_002163) periplasmic protein [Campylobacter jejuni]
MKKIVAIFLVFLGSLWAEDPVIDVVNSGVVLPKIIVKDNSNLSDENLKKSFYNIIVNDLKVSSNFEVVAN
ATETSNYIFEYTLNKNGNTLSLNVKIKAGGSDKSEQTYTLNGLEQYPFLAHKSVKASVNALGLAPVDWMD
HKILIARNSSSKKSQIIMADYTLTYQKVIVDGGLNLFPKWGNKEQTLFYYTAYDHDKPTLYRYDLNTNKA
SKILSSGGMVVASDVNVDGSKLLVTMAPKDQPDVYLYDLNTKNLTQLTNYSGIDVNGNFIGSDDSKVVFV
SDRLGYPNIFMQDLNSNSAEQVVFHGRNNSAVSTYKDFLVYSSREPNQAGVFNIYLMSINSDYIRQLTAN
GKNLFPRFSSDGGSIVFIKYLGAQSALGVIRVNANKTFYFPLRVGKIQSIDW

SEQ ID NO:8
ACE 134 Cj0143
>AnrP57234 (NC_002163) periplasmic solute binding protein for ABC transport system [Campylobacter jejuni]
MKKIILFILSLGIFYTFTQAKNLEQEQNTSSNLVSVSIAPQAFFVKKIAANTLDVNVILPPNSNEHNFEF
KPSTMKKLEKSDIYFTIGLEFEKVFTDKFKQNFPKLQVINMQKNIALIQTHDTHEHSHEHEHHEHGHFDP
HTWLDPILVQTMALNIYDTLIQKYPQNENLYKENLDKFLAELDSLNLQIASKLEKLKNREFVVYHPSWTY
FAKRYNLTQIPVEILGKEPKSKDLQKLITLMKDKNLKVIFVQNGFPENAAKTLAKECDAKIYKIDHLSYD
WENELLKTADAFSHNL

SEQ ID NO:9
ACE 159 Cj0169
>AnrP829849 (NC_002163) superoxide dismutase (Fe) [Campylobacter jejuni]
MFELRKLPYDTNAFGDFLSAETFSYHHGKHHNTYVTNLNNLIKDTEFAGKDLVSIIKTSNGGVFNNAAQV
YNHDFYFDCIKPSTGCGCGGSCQSIDANLQAALEKEFGSLENFKAEFIKGATGVFGSGWFWLVYNTKNQK
LEFVGTSNAATPITEDKVPLLVVDVWEHAYYVDHRNARPAYLEKFYAHINWEFVAKAYEWALKEGMGSVS
FYANELHPVK

SEQ ID NO:10
ACE 183 Cj0193c
>AnrP139712 (NC_002163) trigger factor (peptidyl-prolyl cis /trans isomerase, chaperone) [Campylobacter jejuni]
MEVKAKQLDSVNATASVKIPSGMIKSEVENLAKKASKSVKMDGFRPGKVPVSAVLKRYERELTQDAEQNL
FKSAVNSALQELKKENKELVGEPYFEKFDRKDGEIIAELILSFKPEIKLEGYEKLIPEYQTPKVSKKEID
EKKDELLKRFATPEAIKTKRALKEGDFAKFDFEGFVDDKAFEGGKAENYVLEIGSKQFIPGFEDGMVGMK
IGEEKDIKVTFPKEYGAAHLAGKDAVFKVKLHEIQELKIPELDDEMLKKLLPGEEKASVEVLDEKLKEQI
KNEKLFKLVNDELKGKFADALIEKYNFDLPKGIVEQETDMQMRAAFNTFSEKEIEELKASKEKYQEKRDS
FKEEAQKSVKLTFIIDELAKLRKIEVNDQELIQAIYFEAYRYGMNPKEHLENYKKQGALPAVKMALIEEK
LFNDIFIPKTEKSEKVSKKEKEDK

SEQ ID NO:11
ACE 259 Cj0285c
>AnrP467527 (NC_002163) chemotaxis protein [Campylobacter jejuni]
MFDENIVKTGSNEMELVDFRIFKQGHDKVYEGIYGVNVSKVREIIKIPSLTELPGVPDYIEGIFDLRGVV
IPVVNLAKWMQITEPESTMLKPRVIITEFSNILIGFIVHEAKRIRRINWKDIEPATFSTGSGALDKGKIT
GVTRIENDEVLLILDLESVVEDLGIYAPKTDIDFGKIEKFTGTALILDDSMTARKRVKEMMQQMGFQVVE
AKDGVEGINKLEELSQIYGESLNDTLKIIVSDVEMPQMDGFHFAARIKEDPRFKDIPIVFNSSLSNEFMN
EKGVQEAGGEGYLVKFNASDFFNEIAKVIKKHQSQEQG

SEQ ID NO:12
ACE 332 Cj0358
>AnrP681041 (NC_002163) putative cytochrome C551 peroxidase [Campylobacter jejuni]
MKVKSLLIASLVAFSSLNAASLIDEAKNSGLVALPKDQKGVDEILKQNGVKASEFTLEKAELGKKLYFEP
RLSKSGIISCNTCHNVGLGGTDGISTAIGHKWTANPHHLNSPTVYNAVLNNTQFWDGRAGTLADQAKGPI
QADPEMATPAKLAVEKISSLPEYVSEFKKIYGKSGVNFDNIADAIANFERTLITPSRFDKFLEGDEKALT
KEEQKGLKLFIDKGCVACHNGVNLGGNMQAFEVAGKYKFANLGDFKGDANGMVKTPTLRNVAETAPYFHN
GAIWNLKDAIKEMGSVQLGIKISDKEAKSIETFLKSLTGTKPAIVYPQLPISTEKTPKPEL

SEQ ID NO:13
ACE 419 Cj0448c
>AnrP569688 (NC_002163) putative MCP-type signal transduction protein [Campylobact
MFGSKINHSDLQKLEEENKNLTHKIEKFQSENLELKNKITSLEQAALESKLKTDLLNVLLTGVLKNITII
QGDMLENVNKAEVISSYSKTSLAEMDELNHIANSINASLGNITESANKTRDVAGTLHRSVDEITNVINLI
KDVSDQTNLLALNAAIEAARAGEHGRGFAVVADEVRKLAEKTQKATTEVEMNINLLKQNANEMYTQSEQV
EKISIDSNAHIMSFSEKFTHLVNEAHSTNSNAVGIASEAFVSLAKLDHIAFKLNGYKEIFSKSGKQLADH
TSCRLGKWLASTGKERFGQNKSFLKINEPHEKVHENMNNAITIANTEDISKDITQHSIINKCEVAENASL
DLFNVFKEMLDESDH

SEQ ID NO:14
ACE 420 Cj0449c
>AnrP852550 (NC_002163) hypothetical protein Cj0449c [Campylobacter jejuni]
MLHEYRELMSELKGKDAHFDKLFDRHNELDDMIKDAEEGRTSLSSMEISTLKKEKLHVKDELSQYLANYK
K

SEQ ID NO:15
ACE 481 Cj0511
>AnrP255677 (NC_002163) putative secreted protease [Campylobacter jejuni]
MMELILKTKRFFAGLAGFATTFILCLFLTSHLQAKVDQKEEQVQKRLEALDKLTKTLAIVEQYYVDDQNI
SDLVDKSLSGLLSNLDAHSSFLNEKDFNDMKIQTNGEFGGLGITVGMKDGALTVVSPIEGTPADKAGIKS
GDIILKINDEATLGINLNDAVDKMRGKPKTQITLTIFRKGATKPFDVTLTREIIKIESVYAKMIENENIL
YLRVTNFDKNVVDVASKELKKYPNVKGVILDLRNNPGGLLNQAIGLVNLFVDKGVIVSQKGRIASENQEY
KADPKNKISNASLVVLVNGGSASASEIVSGALQDLKRGVIVGENTFGKGSVQQIIPINKTEALRLTIARY
YLPSGRTIQAVGVKPDIEVFPGKVNTQEDGFSIKESDLKQHLESELEKIDKNKKEDKQENKDNKNLISQK
QINDDAQLKSAIDTIKILNIKQGQ

SEQ ID NO:16
ACE 528 Cj0559
>AnrP252410 (NC_002163) oxidoreductase [Campylobacter jejuni]
MKKIDLIVVGAGPTGIGCAVEAKLKNKEVLILEKSNNICQTLMQFYKDGKRVDKAYKGCEGTNHGHVPFE
DGTKESTIETFQNALKEHNIEVEFGSEVESVKNENGVFLVSTAKGVYECKNIIVAIGRMGKPNKPDYKLP
MTLTKIINFNANSVLGNEKILVVGGGNSAAEYAVDLANSNQVSLCYRKKEFTRLNDINLKDIHEAGNSGK
VELKLGIDINEVEDDNGKAKVNFTDGTSDIYDRIIYAIGGSTPLDFLQKCGINVDDKGVPLMDENKQSNV
KGIFVAGDIATKNGASIVTGLNDAVKILSVL

SEQ ID NO:17
ACE 582 Cj0613
>AnrP916533 (NC_002163) possible periplasmic phosphate binding protein [Campylobac
MKKILSLSVTSLALCGALNAVDLKIAGSSTVYPFTSFVAEEYASIKNTKTPIVESLGTGGGFKVFCEGTT
DISNASRPMKLSEFETCKKAGVTDIVGMMIGYDGIVLAQNKTNAPLNITKKELFLALAKEIPQNGKLIPN
PYTNWNQINKNLPNRKISVYGPPSSSGTRDTIEELVMSDVSKKIPEYKGEYKTIRQDGAYIPSGENDNLI
VSKLTIDKDAFGIFGYSFLVSNSDKINAANIDGVTPSEESIADEKYELARSLFIYINAKKNPKEAFDFAK
IYMSDDLAKSGGELEKIGLVPLSDDKLKASQKHVEDRKILNDELVKAGKVF

SEQ ID NO:18
ACE 605 Cj0636
>AnrP126795 (NC_002163) NOL1\NOP2\sun family protein [Campylobacter jejuni]
MQNILSSFAQEKNVCVFANTLKTSIEELEKEFLKQNLKFKKINVYCYLFDAKDKAILSSMKAFNEAHFYI
QNYSSYLCALNLEVKAGQSVLDMCAAPGGKSINLANFMQNTGYLACNEMSRDRFFILQKNLKNYGVNAKV
FMKDGKNIGNLCPLKFDKILLDAPCSTFAKIGFDLEKSYKEIKNIAKTQKKLLHSALKALKIGGELVYST
CTFTKEENEEVIENALKSEFKLELLDIDLENVEAKAGQSEEFAEISKCRRILPSLDYDGFFIAKLRKLC

SEQ ID NO:19
ACE 667 Cj0706
>AnrP327756 (NC_002163) hypothetical protein Cj0706 [Campylobacter jejuni]
MNKYLEQLVLLSKIDQEIDSYEPKIDSINKTLKDAELKIEKINADLEKIDEEIKDIENQKIQNNAHISEF
SAKIKDLSKKSGVVKTEKEANALKIEEDIAKEQLDAANDEIVRLDKILENKETYKKELEEEKIKQEQNIN
EIRVSIKSEMEVLEKDRMSVYDKKTKLVSEMNQKVLSFYEKIRKWAKNTAVVPVKKQACYGCFMKIYDKT
YLSVVKGEEIVTCPHCGRILYKEQEEQN

SEQ ID NO:20
ACE 676 Cj0715
>AnrP684299 (NC_002163) transthyretin-like periplasmic protein [Campylobacter jeju
MFSIKKTLLILASVPMFLSATEYQLSTHVLDITSGQPAPKVKVELYKLEANQQWKKVSEEFTEENGRIGD
LLPYEKAENRAFGIYKLKFFTKDYYTSHKINTFYPFVEVSFELSKDQKHYHVPITLSPFGYSTYRGS

SEQ ID NO:21
ACE 731 Cj0779
>AnrP191193 (NC_002163) probable thiol peroxidase [Campylobacter jejuni]
MSIVNFKGNPVKLKGNSVEVGADAPKVNLKAKDLSVIEIGAAGKTQIILSVPSLDTPVCATEAREFNKKV
ASYNGAEVIVVSMDLPFAMGRFCSTEGIENLSVASDFVAKEFGEKYGVLINEGALEGLLARAVFVIKEGK
VAYKELVNEITEMPDIAKLDAFFGGSSCCGGCGCH

SEQ ID NO:22
ACE 853 Cj0909
>AnrP318705 (NC_002163) putative periplasmic protein [Campylobacter jejuni]
MKKILLLGALFAVNLWAVNDIEVKNAFVKQTPPHAQNSAIFLTIFNNTNKDIALISAKSDISEVSELHTH
IHKDGKMMMQKIPEIIIKAHSSTELKSGGYHIMLLKLKKPIIKDTKVNLDLKFNNHKTIELKNIDSKEF

SEQ ID NO:23
ACE 937 Cj0994c
>AnrP493933 (NC_002163) ornithine carbamoyltransferase [Campylobacter jejuni]
MKHFLTLRDFSKEEILSLVNHASELKKEPKKLLQDKTLAMIFEKNSTRTRMAFELAITELGGKALFLSSN
DLQLSRGEPVKDTARVIGAMVDFVMMRVNKHETLLEFARYSKAPVINALSELYHPTQVLGDLFTIKEWNK
MQNGIAKVAFIGDSNNMCNSWLITAAILGFEISIAMPKNYKISPEIWEFAMKQALISGAKISLGYDKFEA
LKDKDVVITDTWVSMGEENEKERKIKEFEGFMIDEKAMSVANKDAILLHCLPAYRGYEVSEEIFEKHADV
IFEEARNRLYVVKALLCFLDNQRGRE

SEQ ID NO:24
ACE 941 Cj0998c
>AnrP979073 (NC_002163) putative periplasmic protein [Campylobacter jejuni]
MKKILVSVLSSCLLASALSAVSPKEDSLKISFEGYKTKDMIGTKGEFKNVEYKFSKNIKDLASYLKGAKA
TIKPSNAFMGEGNDIITNNITKVFFPALLGDTDIKVVFQDVIAGENKGVISAKITMDKKSTIVPLTYTIK
DNKFEAKGQLDLHTFKNGSKALKALSDVAAGHGGISWPLVDISFNADLAE

SEQ ID NO:25
ACE 961 Cj1018c
>AnrP257863 (NC_002163) branched-chain amino-acid ABC transport system periplasmic binding protein [Campylobacter jejuni]
MKKSLILASILSLSLSAAEVKIGVVLPLSGATAAYGQSALEGIKLANSMQSALSNGDKVSLAIIDTKGDK
LESSSGANRLVSQDKVIGLIGEMVTANTLQVMRVAEDNKIPLIAPAATGDRLLDKKIYSSRVCFMDSFQG
SSLAKYVFSKLNYKSAVIVVDQSTDYSLGLAKAFEKQYKSNGGQILRILRVNSGDKDFRAIVAQVKSLNP
EFIFLPLYYSEASLFARQSKLAGLNIPMGSADGVADQTFISLAGDASEGYIFTDSFDANNPTTKLSKEFI
SVYEKAKGTKEVPNFSAMGADAYFVMLNAMNACVENLTSKCVNEKIHQTKNYQGVSGVISIDQTGNATRS
VVVKEIKNQKQNYKDIINP

SEQ ID NO:26
ACE 962 Cj1019c
>AnrP326257 (NC_002163) branched-chain amino-acid ABC transport system periplasmic binding protein [Campylobacter jejuni]
MKKLTLTLSVLTMVNCLYAKDINIGVVLPLTGTVAAYGQDVFNGIELANKLQPKLSNGDVIKLITIDTKG
DKLETSNGVNRLIATDKVLGIIGEATTPNTIQAISIAEEKKIPLIAPVASGDKLLDKKKYASRVCFKDSF
QGDKFATYVSKDLGLKNAVIIIDQSNVYSLGLARAFENSFKNNGGKIIKKLVINSGDKDFRAVVSQLKSL
NPDFVYMPIYHPEAALIARQARQIGFDKLLVAGDGVNNQTFIDLGGSAVNGVIFTDSFDYNSPSTQLGKD
FVAAYEKVKGTKELPAFSAMGADAYFVMLNAMNACVDNLSSECINSKIHQTKDFQAVGGVISIDESGNAI
RSVVIKEIQNQKQNYKTIINP

SEQ ID NO:27
ACE 984 Cj1041c
>AnrP198268 (NC_002163) putative periplasmic ATP/GTP-binding protein [Campylobacter jejuni]
MKKYVLSLALLGSLLGASELKYQEFDGFKSPESIFVDKNYVYVSNVGEKLEPLAKDNDGFISKLDKNGKV
LEYKFLTHLNAPKGMMEIGKTLYVVDIDVLRGFDLKTKKEIFNLPIKGAIFLNDIEKLDDNTLLVSDTGT
GLILKVDLKTKQYDELLKLDLAKFGGPNGLYLDRKKHKLFIAGYHPDGVSGGVVMAYDLNTKELSIIKNE
KESYDGIVPYKDGLLVSSWGNNLNGYIYNLDNVKSVKLELPLMKGPADIFIEGNILWIPKMVEGKIFKVE
LNK

SEQ ID NO:28
ACE 1094 Cj1153
>AnrP385049 (NC_002163) putative periplasmic cytochrome C [Campylobacter jejuni]
MKKLLVVSALACLGVSAFAADGATLFKKCAVCHGANADKVYLNKVPALKTLSSAERLQYMKEYSEGKRNA
YGQGAIMKLNLKGLTEEDFKAIEAHIETLK

SEQ ID NO:29
ACE 1155 Cj1214c
>AnrP470247 (NC_002163) hypothetical protein Cj1214c [Campylobacter jejuni]
MFKTIVCFLALNLSLFAVGFDLKPIKSELVKVDDIYGYIKDSDDIKLYSSGVVVQHFSNSQSIIARASVI
DKKNGLAKLEFSVFSALKQDALPLPNVLPKVGDEVVLNFLYDRGLVIAPDEQTYNELVREFPQIYFTHID
IFGAQLIRTATLSPKRSDFRQFCDDNAVGILVVALENHAEVVDCQDFNKLYEVPISKPTSVQVPFYSRIG
GYKSNFFDFNSQEIGNYYRYYDALINLPKVQ

SEQ ID NO:30
ACE 1227 Cj1287c
>AnrP530915 (NC_002163) malate oxidoreductase [Campylobacter jejuni]
MNLKEEALKYHLGGKIDIVPSKPMATSYDLSLAYSPGVAEPCLEIAKDNELAYTYTNKANLVAIVSDGSA
VLGLGNIGAQASKPVMEGKACLFKKFANVNAYDIEINVHSIEEIVNFCKALAPTVGGINLEDIAAPKCFE
IEAALQDLGIPVMHDDQHGTAIISTAGLMNAMEISGKKFKDIKVVVSGAGAAGIASAKMYRNLGVENIIL
VDSKGVISKDRNDLTPQKLEFAVDSKEKTLKEVLKGADVFLGLSAPKILDDEMVLSMAKDPVIFALANPI
PEVMPEDVARLRKDAIVGTGRSDYPNQINNVLGFPFIFRGALDVRASKITENMKVAAAKALADLAKLPVS
DAVKKAYNLSTLEFGRDYVIPKPFDERVKAAVSTAVAAAAVKDGVAKVKNFDEKAYFESLK

SEQ ID NO:31
ACE 1320 Cj1380
>AnrP108083 (NC_002163) putative periplasmic protein [Campylobacter jejuni]
MKKLSLILVCSASLFAASNSEISDFYSKSIKAQFPNATVSVSNRQKVGNTGFESVIVSVELNGQKQENIL
FTKDSLITPDLIDLKTGISYAQEYEMKKFQEARENFTKNAKAVAQKETMVIALGDKNKPAIYVFSDPECP
YCREHLAQIDDELKNYQVNYILTPVHGKSAFEKSALIYKEAKKAKNDKEKIAILNKYYDANIKNYPKVSD
AELKEVFSLYEKYRSLGLSATPTIIK

SEQ ID NO:32
ACE 1431 Cj1496c
>AnrP947055 (NC_002163) putative periplasmic protein [Campylobacter jejuni]
MIKKFILLVFISSVVFGAEQDCEQYFEARKAQIELQTREFDEARQSLEAYKASFEALQKERLENLEKKEA
EVNATLAKIEELKLENARLVEEQQKILNSINDKTQGRVKEIYSQMKDAAIADVLSQMDAEDASKIMLSLE
SRKISGVLSKMDPKKASELTLLLKNLDNNASN

SEQ ID NO:33
ACE 1449 Cj1516
>AnrP407504 (NC_002163) putative periplasmic oxidoreductase [Campylobacter jejuni]
MNRRNFLKFNALTLASMGVAYANPMHDMHSMHKNHSINHDLDTSFINFAPKNLKLLDPKQFPQGEILKAL
PLLKNESKEKNIFRATLEIKENHIELIKGKKTLFYTYNGLVPAPKIEVFEGDKLEILVKNKLKEATTIHW
HGVPVPPDQDGSPHDPILAGEERIYRFEIPQDSAGTYWYHPHPHYTASKQVFMGLAGAFVIKAKKDALSH
LKEKDLMISDLRLDENAQIPNNNLNDWLNGREGEFVLINGQFKPKIKLATNERIRIYNATAARYLNLRIQ
GAKFILVGTDGGLIEKAIYKEELFLSPASRVEVLIDAPKDGNFKLESAYYDRDKMMVKEESNTLFLANIN
LKKEKLELPKNLKIFKPLEEPKEFKEIIMSEDHMQMHGMMGKSENELKIALASMFLINGKSYDLKRIDLS
SKLGVVEDWIVINKSHMDHPFHIHGTQFELISSKLNGKVQKAEFRAFRDTINVRPNEELRLKMKQDFKGL
RMYHCHILEHEDLGMMGNLEVKE

SEQ ID NO:34
ACE 1469 Cj1540
>AnrP818860 (NC_002163) putative periplasmic protein [Campylobacter jejuni]
MKKIISLALALALSASAAELKMATTTSTDNTGLLDALKPLYEKESGNTLKWVAVGTGAALKMGEDCNADV
LFVHSPKAEKEFMKKGFGVDRTPVMYNDFIIIADKSLASKFKGKNLKESLELIKNEKLTFISRGDKSGTD
NKEKSLWKNLGGVPEKQSWYQQSGQGMLASIKIAEEKKGVILTDRGTYIKYEANEKGKPNLVIVNEGDDS
LKNFYSVIATNPKHCKNVNYTEASKFIKWVTSDKTLNFIADFKLLNKPLFVIDAKTRKD

SEQ ID NO:35
ACE 1584 Cj1659
>AnrP294550 (NC_002163) periplasmic protein p19 [Campylobacter jejuni]
MIKKVLSVVAAAAVISTNLFAGEVPIGDPKELNGMEIAAVYLQPIEMEPRGIDLAASLADIHLEADIHAL
KNNPNGFPEGFWMPYLTIAYELKNTDTGAIKRGTLMPMVADDGPHYGANIAMEKDKKGGFGVGNYELTFY
ISNPEKQGFGRHVDEETGVGKWFEPFKVDYKFKYTGTPK

SEQ ID NO:36
ACE 1569 Cj1643
>AnrP407676 (NC_002163) putative periplasmic protein [Campylobacter jejuni]
MKKILIICMLFTLSFGIERPKFEDFLAGYERNKASMLNYEGMPAFALSENLLAVLKQPNAKLNKYVKYDP
FLNLYLVRTDFSLIPTPMGDEEKLTRNDWVGIWDPNKPYIGHIKYLAQNIDEKDQLDFNSKIGLLGTPCC
EMMGIALNNSSFIGNRYLKHFMKYNDVYWGDIGVDFVVRENKIYVNNVRKNPQFLINDQVISVDGLPAND
LRKLNEKILFADRGSTLYFQVLRDNMDLNISTEVFAKDLSKFNLPDSKPKPKITNFTSNLGLTVNASLVV
TKIDPKSKVSNAGFMVGDKILRVNNIILNNFKELQNILSAGNDFSILIERKSTKLPLSNFNNELGGNANS
GGDGKFQFFIRLTK

SEQ ID NO:37
ACE 96 Cj0105
>AnrP758295 (NC_002163) ATP synthase F1 sector alpha subunit [Campylobacter jejuni
MKFKADEISSIIKERIENFDLNLEIEETGKIISVADGVAKVYGLKNIMAGEMVEFENGDKGMALNLEESS
VGIVILGKGEGLKEGASVKRLKKLLKVPVGEALIGRVVNALGEPIDAKGVINANEYRFVEEKAKGIMARK
SVHEPLHTGIKAIDALVPIGRGQRELIIGDRQTGKTTVAVDTIISQRGQGVICIYVAIGQKQSTVAQVVK
RLEEHGAMEYTIVVNAGASDPAALQYLAPYTGVTMGEFFRDNAKHALIVYDDLSKHAVAYREMSLILRRP
PGREAYPGDVFYLHSRLLERASKLNDELGAGSLTALPIIETQAGDVSAYIPTNVISITDGQIFLETDLFN
SGIRPAINVGLSVSRVGGAAQIKATKQVSGTLRLDLAQYRELQAFAQFASDLDEASRKQLERGQRMVELL
KQPPYSPLSVEKQVVLIFAGTKGFLDDIAVSRIKEFEDGIYPFIEAKHPDIFEQIRSKKALDSDLEEKLA
KAINEFKANHL

SEQ ID NO:38
ACE 165 Cj0175
>AnrP550554 (NC_002163) putative iron-uptake ABC transport system periplasmic iron
MKKIFFMFLTAVSFLGASELNIYSARHYNADFEIIKKFEEKTGIKVNHTQAKASELIKRLSLEGSNSPAD
IFITADISNLTEAKNLGLLSPVSSKYLEEFIPAHLRDKDKEWFAITKRARIIAYNKNTNIDISKMKNYED
LAKAEFKGEIVMRSATAPYSKTLLASIIANDGNKEAKAWAKGVLENLATNPKGGDRDQARQVFAGEAKFA
VMNTYYIGLLKNSKNPKDVEVGNSLGIIFPNQDNRGTHINISGIAMTKSSKNQDAAKKFMEFMLSPEIQK
ILTDSNYEFPIRNDVELSQTVKDFGTFKEDQIPVSKIAENIKEAVKIYDEVGFR

SEQ ID NO:39
ACE 257 Cj0283c
>AnrP602342 (NC_002163) chemotaxis protein [Campylobacter jejuni]
MSNEKLEQILQKQQTQMAGPDVDQREDDIIQLVGFVVGDEEYAIPILNIQEIIKPIEYTRVPSVPDYVLG
VFNMRGNVMPLIDLAQRFHLGSSKMTPQTRYIVLRGETNGTGVGGNAGFVIDRLTEAIKIHRNRIDPPPE
TLVKDKGMIYGIGKRDENILTILKVEALLKREF

SEQ ID NO:40
ACE 277 Cj0303c
>AnrP311344 (NC_002163) putative molybdate-binding lipoprotein [Campylobacter jejuni]
MKKFVVFFGILLFVSCLNAQNLSIFVASSASKAMSEVKDEFLKTHPEDKIELVFGASGKYYELLKQGREF
DLFFSADTKYAKAIYDDKNALIKPKVYVLGVLALYSLDENLLQGGVENLKEKANKITHLSIANPKVAPYG
VAAKEVLENLGLNELLKDKIVLGENISVPVLHVDSKNSDIAIVAYSLVSSINHPKGKAVIIDAKYFSPLE
QSYVITKYAKDKKLAFEFNEFIGSSKAKEIFKKYGFSTP

SEQ ID NO:41
ACE 308 Cj0334
>AnrP505685 (NC_002163) alkyl hydroperoxide reductase [Campylobacter jejuni]
MIVTKKALDFTAPAVLGNNEIVQDFNLYKNIGPKGAVVFFYPKDFTFVCPSEIIAFDKRYQEFKNRGIEV
IGISGDNEFSHFAWKNTPVNQGGIGQVKFPLVADLTKQIARNFDVLYAEAVALRGSFLLDADGTVRHAVV
NDLPLGRNIDEMLRMVDTMLFTNEHGEVCPAGWNKGDEGMKANPKGVAEYLGKNEAKL

SEQ ID NO:42
ACE 388 Cj0415
>AnrP72219 (NC_002163) putative oxidoreductase subunit [Campylobacter jejuni]
MAEVLKKVDVVTVGAGWTGGIVAAELTKAGLNVLSLERGHMQSTENFNYIHDEWRYGINYGLMQDCSKDT
VTFRHDPSGLALPYRKMGSFLLGNNVGGAGVHWNGWTFRFMPYDFEIQTLSKQRYGNKLGNDYTLQDWGV
TYKDMEPYYDRFEKTCGVSGEPNPLAEKMGAFRSSPYPQEPLENTKMLKRFESAAKSSNLHTYRLPASNS
KGGYTNPDGQDLAPCQYCAYCERFGCEYGAKASPLNTVIPKAMSTGKYTIRTYSNVTQILKKDGKVTGVK
FVDTRTMKEYIQPADIVVLTSYMFNNAKLLMVSNIGEQYDPKTGKGTLGRNYCYQMNMGTTAFFDEQFNT
FMGSGALGTTSDDFNGDNFDHSKEKFLHGAMIYSVQLGTRPIQSAPLPAGAPTWGAEFKKALNYNFTRAI
TVGGQGASLPHKNNYLSLDPTYKDAFGMPLLRLTYNFTDQDRALHKFITDKTAEVAKRMQGVKSIKKGAY
LKDYSVVPYQSTHNTGGTTMGADRETSVVNTYLQHWDADNLFVVGAGNFQHNSGYNPTDTVGALAYRCAE
GILKYHKSGKSLA

SEQ ID NO:43
ACE 393 Cj0420
>AnrP490750 (NC_002163) putative periplasmic protein [Campylobacter jejuni]
MKKVLLSSLVAVSLLSTGLFAKEYTLDKAHTDVGFKIKHLQISNVKGNFKDYSAVIDFDPASAEFKKLDV
TIKIASVNTENQTRDNHLQQDDFFKAKKYPDMTFTMKKYEKIDNEKGKMTGTLTIAGVSKDIVLDAEIGG
VAKGKDGKEKIGFSLNGKIKRSDFKFATSTSTITLSDDINLNIEVEANEK

SEQ ID NO:44
ACE 711 Cj0759
>AnrP586832 (NC_002163) heat shock protein dnaK [Campylobacter jejuni]
MSKVIGIDLGTTNSCVAVYERGESKVIPNKEGKNTTPSVVAFTDKGEVLVGDSAKRQAVTNPEKTIYSIK
RIMGLMINEDAAKEAKNRLPYHITERNGACAIEIAGKIYTPQEISAKVLMKLKEDAEAFLGESVTDAVIT
VPAYFNDAQRKATKEAGTIAGLNVLRIINEPTSAALAYGLDKKDSEKIVVYDLGGGTFDVTVLETGDNVV
EVLATGGNAFLGGDDFDNKLIDFLANEFKDETGIDLKNDVMALQRLKEAAENAKKELSSANETEINLPFI
TADASGPKHLVKKLTRAKFEGMIDSLVAETITKINEVVSDAGLKKDEIKEIVMVGGSTRVPLVQEEVKKA
FNKDLNKSVNPDEVVAIGAAIQGAVIKGDVKDVLLLDVTPLSLGIETLGGVMTKIIEKGTTIPTKKEQVF
STAEDNQSAVTINVLQGEREFSRDNKSLGNFNLEGIPPAPRGMPQIEVTFDIDANGILTVSAKDKATGKA
QEIKITGSSGLSEEEINNMVKDAELHKEEDKKRKEAVDARNAADSLAHQVEKSLSELGEKVAAADKENIQ
KALDDLRETLKNQNASKEEIESKMKALSEVSHKLAENMYKKDEPNTANDKKKKDDDVIDAEVE

SEQ ID NO:45
ACE 723 Cj0771c
>AnrP524051 (NC_002163) putative periplasmic protein [Campylobacter jejuni]
MNLFKIIILACILNLSSLFAQNITIGATPNPFGSLLELMKDDFKNKGYELKIVEFSDYILPNRALEEKEL
DANLYQHKPFLEEYNLKKGSNLIATTPVLIAPVGVYSKKIKNLENLKEGARVAIPNDATNESRALELLEK
AKLIELNKNTLKTPLDINKNPKKLKFIELKAAQLPRALDDVDIAIINSNFALGAGLNPSKDTIFREDKNS
PYVNYVVVRSEGKNSEKTKVIDEILRSDKFKAIINEHYKDILIPAF

SEQ ID NO:46
ACE 724 Cj0772c
>AnrP579672 (NC_002163) putative periplasmic protein [Campylobacter jejuni]
MKIKSLFIASILTLSLNANALETITVAATPVPHAEILEQVKPDLEKQGYKLEIKEFTDYVLPNLAVDNGE
ADANFFQHTPYLEEFNKNKGTKLIKVAAIHIEPMAVYSKKYKSLDDIKEGVKIAIPNDPTNESRALDIIA
KKGLVKFKDKALKTPLDIIDNPKKIKFVELKPAQLPRALNDVDFAVINSNYALSANLNPAKDSVFIEDKE
SPYANILVVRVGHENDPKIKALIQALQSDKIKQFIIEKYNGSVLPAF

SEQ ID NO:47
ACE 819 Cj0872
>AnrP694298 (NC_002163) putative protein disulphide isomerase [Campylobacter jejun
MRNFFCKFVLALVFYSSFALANNSFITLNPSLPSSENSVIEAFSYKCIHCYNHHKFGTLEKLREAFPNLH
FKLYPVSLMNGEFSKEMNELFTFAQYKDEQNGKDASYSDSLSHKLADVYFVSYFLNKQRNFSNLDEFYDI
GLKAMNVNKNEVLNFLNTPKAKEILSEFQRANDIAKTYGTPAFVVNGKYQINPSAINSMQDLEDLVKKLS
NMK

SEQ ID NO:48
ACE 1060 Cj1118c
>AnrP515430 (NC_002163) chemotaxis regulatory protein [Campylobacter jejuni]
MKLLVVDDSSTMRRIIKNTLTRLGHDDVLEAEHGVEAWDLLTKNEDVKVLITDWNMPEMNGLELVKKVRA
EKKYEDMPIIMVTTEGGKAEVITALKAGVNNYIVKPFTPQVLKEKLEDVLGTGSGEGAAE

SEQ ID NO:49
ACE 1169 Cj1228c
>AnrP679791 (NC_002163) serine protease (protease DO) [Campylobacter jejuni]
MKKIFLSLSLASALFAASINFNESTATANRVNPAAGNAVLSYHDSIKDAKKSVVNISTSKTITRANRPSP
LDDFFNDPYFKQFFDFDFSQRKGKNDKEVVSSLGSGVIISKDGYIVTNNHVVDDADTITVNLPGSDIEYK
AKLIGKDPKTDLAVIKIEANNLSAITFTNSDDLMEGDVVFALGNPFGVGFSVTSGIISALNKDNIGLNQY
ENFIQTDASINPGNSGGALVDSRGYLVGINSAILSRGGGNNGIGFAIPSNMVKDIAKKLIEKGKIDRGFL
GVTILALQGDTKKAYKNQEGALITDVQKGSSADEAGLKRGDLVTKVNDKVIKSPIDLKNYIGTLEIGQKI
SLSYERDGENKQASFILKGEKENPKGVQSDLIDGLSLRNLDPRLKDRLQIPKDVNGVLVDSVKEKSKGKN
SGFQEGDIIIGVGQSEIKNLKDLEQALKQVNKKEFTKVWVYRNGFATLLVLK

SEQ ID NO:50
ACE 1510 Cj1584c
>AnrP355324 (NC_002163) putative peptide ABC-transport system periplasmic peptide-
MLRWFVLLFLLFLNLEAKIPKDTLIIAVENEIARINPAYSEDHDAVINLVFSGLTRFDENMSLKPDLAKS
WDISKDGLVYDIFLRDDVLWHDGVKFSADDVKFSIEAFKNPKNNSSIYVNFEDIKSVEILNPSHVKITLF
KPYPAFLDALSIGMLPKHLLENENLNTSSFNQNPIGTGPYKFVKWKKGEYVEFKANEHFYLDKVKTPRLI
IKHIFDPSIASAELKNGKIDAALIDVSLLNIFKNDENFGILREKSADYRALMFNLDNEFLKDLKVRQALN
YAVDKESIVKNLLHDYAFVANHPLERSWANSKNFKIYKYDPKKAEDLLVSAGFKKNKDGNFEKDGKILEF
EIWAMSNDPLRVSLAGILQSEFRKIGVVSKVVAKPAGSFDYSKVDSFLIGWGSPLDPDFHTFRVFESSQD
SALNDEGWNFGHYHDKKVDIALQKARNTSNLEERKKYYKDFIDALYENPPFIFLAYLDFALVYNKDLKGI
KTRTLGHHGVGFTWNVYEWSK

SEQ ID NO:51
ACE 1543 Cj1617
>AnrP111949 (NC_002163) putative haemin uptake system periplasmic haemin-binding protein [Campylobacter jejuni]
MKKILIIMSLFLIALNAKERLVVLDPASIETLFMLKAEDQIVGIATLQHSNIYPKDQTSKLTSVGTFSNP
SLEKIVALKPSLVILSSYSLNLEEGLKNFGIKSINLKAERLEDITKNITTLGQITKKEKEAELLKQEFNQ
KFKKLSDKPLNKSAIYLYSSNPLMAFNDNSLIADILRLIGIKNLSPQSQISRPVISAEYILKQNPDILIL
GINAKNNLLDTNALLKNTKAVKTGSIYFNKDTPILLRLSPKIIDRIQEFKTKLENNNF

Fragments of AnrP630851 (Cj0092)
SEQ ID NO:52: TQQDINTQNEMSDASTKDITPKSIEDFFEEFAD
SEQ ID NO:53: GITKDGKTFYTGKSTVAVNDTDPQF
SEQ ID NO:54: RIATSKIQNYEADNSTNAKEFDELPKGDKVDQILNK
SEQ ID NO:55: QLDKALKDLGIDTNSLSEDRKKTLLKQEFLNKTMTN
SEQ ID NO:56: TIVTQRRGEYDVGVVAVISNKTRQLAKD
SEQ ID NO:57: AISEYLPKDTKGFLNEYGIRLVYDEN
SEQ ID NO:58: DPSNAKKTNILEDRAKET
SEQ ID NO:59: LSLKDERTTGDTYEEII
SEQ ID NO:60: VNDSSTQEQTQNITN
SEQ ID NO:61: TLKKWSYTSENG
SEQ ID NO:62: YSYENLANTNEALNSKSNATKNEAKKSSSIQRS

Fragments of AnrP57234 (Cj0143c)
SEQ ID NO:63: IFYTFTQAKNLEQEQNTSSNLVSVS
SEQ ID NO:64: LPPNSNEHNFEFKPSTMKKLEKSDIYF
SEQ ID NO:65: LEFEKVFTDKFKQNFPKLQVINMQ
SEQ ID NO:66: IQTHDTHEHSHEHEHHEHGHFDPHTWL
SEQ ID NO:67: DTLIQKYPQNENLYKENLDK
SEQ ID NO:68: SKLEKLKNRE
SEQ ID NO:69: YFAKRYNL
SEQ ID NO:70: GKEPKSKDLQK
SEQ ID NO:71: LMKDKNLK
SEQ ID NO:72: QNGFPENAAKTLAKECDAKIYK
SEQ ID NO:73: DHLSYDWENELLKTADAF

Fragments of AnrP490750 (Cj0420)
SEQ ID NO:74: FAKEYTLDKAHTDVGFKIKHLQI
SEQ ID NO:75: VKGNFKDYSAVIDFDPASAEFKKLDVTI
SEQ ID NO:76: SVNTENQTRDNHLQQDDFF
SEQ ID NO:77: DFFKAKKYPDMTFTM
SEQ ID NO:78: TFTMKKYEKIDNEKGKMT
SEQ ID NO:79: GVAKGKDGKEKIGF
SEQ ID NO:80: LNGKIKRSDFKFATS
SEQ ID NO:81: EVEANEK

Fragments of AnrP684299 (Cj0715)
SEQ ID NO:82: LSATEYQLSTHV
SEQ ID NO:83: ITSGQPAPKVKVELYK
SEQ ID NO:84: LEANQQWKKVSEEFTEENGRIG
SEQ ID NO:85: LLPYEKAENRAFG
SEQ ID NO:86: KFFTKDYYTSHKINTF
SEQ ID NO:87: SFELSKDQKHYHVPI
SEQ ID NO:88: FGYSTYRGS

Fragments of AnrP579672 (Cj0772c)
SEQ ID NO:89: ILEQVKPDLEKQGYKLEIKEFTDY
SEQ ID NO:90: GEADANFFQHTPYLEEFNKNKGT
SEQ ID NO:91: AVYSKKYKSLDDIKE
SEQ ID NO:92: IPNDPTNESRAL
SEQ ID NO:93: KGLVKFKDKALKTPLDIIDNPKKIKFVELKPAQLPRALN
SEQ ID NO:94: ANLNPAKDSVFIEDKESPYAN
SEQ ID NO:95: GHENDPKIKALIQALQSDKIKQFIIEKYN

Fragments of AnrP257863 (Cj1018c)
SEQ ID NO:96: NGDKVSLAIIDTKGDKLESSSGANRLVSQDK
SEQ ID NO:97: VAEDNKIPLIAPAATGDRLLDKKIYSSRVC
SEQ ID NO:98: YVFSKLNYKSAVIVVDQSTDYSLGLAKAFEKQYKSNGGQ
SEQ ID NO:99: NSGDKDFRAIVAQVKSLNPEFIFLPLYYSEASLFARQSKLA
SEQ ID NO:100: GYIFTDSFDANNPTTKLSKEFISVYEKAKGTKEVPNFSAMG
SEQ ID NO:101: VNEKIHQTKNYQGVS
SEQ ID NO:102: QTGNATRSVVVKEIKNQKQNYKDIIN

Fragments of AnrP108083 (Cj1380)
SEQ ID NO:103: ELNGQKQENILFTK
SEQ ID NO:104: SYAQEYEMKKFQEARENFTKNAKAVAQKETM
SEQ ID NO:105: VIALGDKNKPAI
SEQ ID NO:106: HLAQIDDELKNYQV
SEQ ID NO:107: YKEAKKAKNDKEKIAI
SEQ ID NO:108: LNKYYDANIKNYPKVSDAELKEVFSLYEKYRSL

Fragments of AnrP407676 (Cj1643)
SEQ ID NO:109: GIERPKFEDFLAGYERNKASMLN
SEQ ID NO:110: LKQPNAKLNKYVKYDPFL
SEQ ID NO:111: PTPMGDEEKLTRNDWVGIWDPNKPYI
SEQ ID NO:112: AQNIDEKDQLDFNSK
SEQ ID NO:113: GNRYLKHFMKYNDVY
SEQ ID NO:114: VVRENKIYVNNVRKNPQFL
SEQ ID NO:115: PANDLRKLNEK
SEQ ID NO:116: DRGSTLYFQVLRDNMDLN
SEQ ID NO:117: AKDLSKFNLPDSKPKPKI
SEQ ID NO:118: TKIDPKSKVSNAG
SEQ ID NO:119: LIERKSTKLPLSNFN

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